low in animals that survived. Exogenous administration of recombinant mouse IL-6 reversed the immunogens' protective effects. Protection against infection in mice does not necessarily correlate with the measured levels of serum bactericidal **antibody** alone, opsonic **antibody** alone, or cytokine profile alone. A comprehensive assessment of the preclinical efficacy of group B outer-membrane protein vaccines should include monitoring humoral **antibodies**, cytokine response, and protective effects against lethal infection.

L25 ANSWER 10 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 97333138 EMBASE
DOCUMENT NUMBER: 1997333138
TITLE: Phase variation and conservation of **lipooligosaccharide** epitopes in Haemophilus somnus.
AUTHOR: Inzana T.J.; Hensley J.; McQuiston J.; Lesse A.J.; Campagnari A.A.; Boyle S.M.; Apicella M.A.
CORPORATE SOURCE: T.J. Inzana, Ctr. for Molec. Med./Infectious Dis., Virginia-Maryland RCVM, Virginia Polytech. Inst./State Univ., Blacksburg, VA, United States. tinzana@vt.edu
SOURCE: Infection and Immunity, (1997) 65/11 (4675-4681). Refs: 36
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The bovine-specific **pathogen** Haemophilus somnus is capable of undergoing structural and antigenic phase variation in its **lipooligosaccharide** (**LOS**) components after in vivo and in vitro passage. However, commensal isolates from the reproductive tract have not been observed to vary in phase iT. J. Inzana, R. P. Gogolewski, and L. B. Cotbell, Infect. Immun. 60:2943-2951, 1992). We now report that specific monoclonal **antibodies** (MAbs) to the LOSs of Haemophilus aegyptius, **Neisseria gonorrhoeae**, and Haemophilus influenzae, as well as H. somnus, reacted with some phase-variable epitopes in H. somnus **LOS**. All reactive MAbs bound to **LOS** components of about 4.3 kDa in the same H. somnus isolates, including a non-phase-varying strain. Following in vitro passage of a clonal variant of strain 738 that was nonreactive with the MAbs. 11.8% of young colonies shifted to a reactive phenotype. A digoxigenin- labelled 5'-CAATCAATCAATCAATCAATCAATCAAT-3' oligo-nucleotide probe hybridized to genomic DNA from strain 738 but did not react with DNA from a non-phase- varying strain. Sequence analysis of the gene containing 5'-CAAT-3' tandem sequences revealed 48% amino acid homology with the lex-2B gene-encoded protein of H. influenzae **type b**. Our results indicate that some **LOS** epitopes are conserved between H. somnus and other Haemophilus and **Neisseria** species, that **LOS** phase variation may occur at a high rate in some strains of H. somnus, and that phase variation may, in part, be due to 5'-CAAT-3'

tandem sequences present in H. somnus genes.

L25 ANSWER 11 OF 27 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 97378095 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9234776
TITLE: Neisserial porins may provide critical second signals to polysaccharide-activated murine B cells for induction of immunoglobulin secretion.
AUTHOR: Snapper C M; Rosas F R; Kehry M R; Mond J J; Wetzler L M
CORPORATE SOURCE: Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814, USA.. Snapper@usuhs.usuhsb.mil
CONTRACT NUMBER: AI32560 (NIAID)
SOURCE: Infection and immunity, (1997 Aug) 65 (8) 3203-8. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970825
Last Updated on STN: 19970825
Entered Medline: 19970814

AB Resting B cells stimulated with dextran-conjugated anti-immunoglobulin D (anti-IgD) **antibodies** (anti-Ig-dex), a model for B-cell activation in response to polysaccharide antigens, proliferate but secrete little if any Ig, unless additional stimuli are present. In order to elucidate the parameters which costimulate T-cell-independent antipolysaccharide **antibody** responses during bacterial infections, we tested the capacities of highly purified porin proteins from Neisseria meningitidis and Neisseria **gonorrhoeae** to augment in vitro proliferation and induce Ig secretion by anti-Ig-dex-activated B cells. Resting B cells, from **lipopolysaccharide** (**LPS**)-nonresponsive C3H/HeJ mice, proliferated and secreted IgM in response to each of three distinct porins acting alone. Further, porins, even at concentrations that were minimally inductive when acting alone, were strongly synergistic with anti-Ig-dex for proliferation and Ig secretion. Similar synergistic effects of porins with CD40-ligand were also observed. These effects of porins were shown to occur directly at the level of the B cell. The predominant Ig isotype elicited in response to porins plus anti-Ig-dex or CD40-ligand was IgM (>97%), with the remainder comprising IgG. Surprisingly, picogram-per-milliliter amounts of neisserial **LPS** were also found to be highly synergistic with anti-Ig-dex for induction of IgM secretion by **LPS** -responsive C3H/HeN, but not C3H/HeJ, B cells. Thus, these data suggest that porins, as well as **LPS**, may provide critical second signals for T-cell-independent induction of ' polysaccharide-specific Ig in response to **neisserial** and other gram-negative porin-expressing bacterial **pathogens**, without a requirement for the participation of non-**B** cell **types**. These data may also help to explain the potent immunopotentiating effects of porins for polysaccharide-specific, as well as protein-specific, humoral responses in vivo.

L25 ANSWER 12 OF 27 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 97:39145 DISSABS Order Number: AARNN14455
TITLE: MOLECULAR CHARACTERIZATION OF GENES INVOLVED IN PASTEURELLA HAEMOLTYICA A1 LIPOPOLYSACCHARIDE BIOSYNTHESIS
AUTHOR: POTTER, MIRIAM DEBORAH [PH.D.]; LO, REGGIE Y. C. [advisor]
CORPORATE SOURCE: UNIVERSITY OF GUELPH (CANADA) (0081)
SOURCE: Dissertation Abstracts International, (1996) Vol. 57, No. 12B, p. 7348. Order No.: AARNN14455. 254 pages. ISBN: 0-612-14455-0.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19970507
Last Updated on STN: 19970507

AB This thesis describes molecular characterization of genes involved in lipopolysaccharide (LPS) biosynthesis in Pasteurella haemolytica A1, a Gram-negative veterinary **pathogen**. Two genes involved in LPS biosynthesis were cloned by expression in a heterologous host. The product of the first gene isolated, lpsA, was able to modify the rough LPS core of Escherichia coli K-12. lpsA sequences were detected in all twelve serotypes of P. haemolytica by PCR amplification and Southern blot hybridization. LpsA shares 45% overall sequence similarity with Lex-1, and 48% overall sequence similarity with LgtE. Lex-1 and LgtE are lipooligosaccharide biosynthetic enzymes from Haemophilus influenzae **type b**, and **Neisseria gonorrhoeae** and N. **meningitidis**, respectively. LpsA, together with Lex-1 and LgtE, are proposed to represent a novel family of LOS biosynthetic genes found in mucosal **pathogens**. The second gene isolated, **galE**, was cloned by complementation of a Salmonella enterica serovar Typhimurium **galE** mutant. The deduced amino acid sequence of the P. haemolytica A1 **GalE** shares 82% overall sequence similarity with the **GalE** of H. influenzae **type b** and over 73% overall sequence similarity with the **GalE** enzymes of N. **gonorrhoeae** , N. **meningitidis**, and Yersinia enterocolitica. The P. haemolytica A1 **galE** was not found as part of the classical galactose operon. Sequences homologous to the P. haemolytica A1 **galE** were detected in the twelve serotypes of P. haemolytica, the four serotypes of P. trehalosi, Actinobacillus suis, A. pleuropneumoniae and E. coli by Southern blot hybridization. lpsA and **galE** gene functions were inactivated by insertion of antibiotic resistance cassettes into their coding sequences. Optimal electroporation conditions were determined for the introduction of DNA into P. haemolytica A1. Conditions of 25 $\mu\rm F$ capacitance, 600 Ω resistance, and 15.0 $\rm kV{\cdot}cm\sp{-1}$ field strength, followed by a recovery period of six hours, resulted in a maximum electroporation efficiency of $5.2\times10\sp5$ transformants per $\mu\rm g$ of DNA. Electroporation of the inactivated **galE** gene construct carried on a suicide vector resulted in a single crossover event with the integration of the entire suicide vector but without

subsequent excision of the chromosomal wild type copy of the **galE** gene.

L25 ANSWER 13 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 96368841 EMBASE
DOCUMENT NUMBER: 1996368841
TITLE: Outer membrane protein of Neisseria meningitidis as a mucosal adjuvant for **lipopolysaccharide** of Brucella melitensis in mouse and guinea pig intranasal immunization models.
AUTHOR: Van de Verg L.L.; Hartman A.B.; Bhattacharjee A.K.; Tall B.D.; Yuan L.; Sasala K.; Hadfield T.L.; Zollinger W.D.; Hoover D.L.; Warren R.L.
CORPORATE SOURCE: Department of Bacterial Diseases, Walter Reed Army Research Institute,Washington, DC 20307, United States
SOURCE: Infection and Immunity, (1996) 64/12 (5263-5268). ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A mucosal vaccine against brucellosis consisting of the **lipopolysaccharide** (**LPS**) of Brucella melitensis complexed with the outer membrane protein (GBOMP) of **group B Neisseria meningitidis** was tested in small-animal models of intranasal immunization. Mice given two doses of the vaccine developed high levels of immunoglobulin G (IgG) and IgA **antibodies** specific for B. melitensis **LPS** in lung lavages and specific IgG and IgA **antibody**-secreting cells in the lungs and spleen. Similarly, in guinea pigs immunized twice intranasally, IgG and IgA **LPS**-specific **antibodies** were detected in lung lavages, and specific **antibody**-secreting cells were isolated from the spleen and cervical nodes. In mice immunized with **LPS** only, pulmonary responses consisted mostly of IgM **antibodies**, while guinea pigs given **LPS** alone developed local **antibody** of all three isotypes, but at lower levels compared to animals given the complex vaccine. Both mice and guinea pigs also developed high levels of serum IgG and moderate levels of IgA as a result of intranasal immunization with the complex vaccine. The serum **antibodies** in both cases were found to cross-react with the **LPS** of B. abortus, which shares an immunogenic epitope with B. melitensis **LPS**. In mice given the complex vaccine, there was a prominent serum IgG1 response that was absent in the mice given **LPS** alone. In conclusion, the N. **meningitidis** GBOMP was an effective mucosal adjuvant for secretory IgA and IgG responses in the lungs of both mice and guinea pigs. The IgG1 subclass response in mice suggests that GBOMP may have favored a Th2 type of response to the **LPS**. A vaccine capable of stimulating high levels of **antibody** at local

sites has the potential to protect against brucellae, since these **pathogens** gain entry to the host via mucosal routes.

L25 ANSWER 14 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96066942 EMBASE
DOCUMENT NUMBER: 1996066942
TITLE: Cloning and characterization of the **galE** locus of Pasteurella haemolytica A1.
AUTHOR: Potter M.D.; Lo R.Y.C.
CORPORATE SOURCE: Department of Microbiology, Canadian Bacterial Diseases Network, University of Guelph,Guelph, Ont. N1G 2W1, Canada
SOURCE: Infection and Immunity, (1996) 64/3 (855-860). ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The enzyme UDP-galactose 4-epimerase (**GalE**) is involved in one of the major steps of galactose metabolism in bacteria. In many cases, **GalE** is required for the biosynthesis of extracellular polysaccharide materials such as lipopolysaccharide (LPS) and capsule. Mutants defective in **galE** have been shown to exhibit reduced virulence. Here we describe the cloning and characterization of the **galE** gene from the bovine **pathogen** Pasteurella haemolytica A1. This was achieved by the complementation of a Salmonella typhimurium **galE** mutant with a P. haemolytica A1 plasmid bank. Analysis of six clones recovered on minimal media with galactose as the carbon source showed that they all contained the same recombinant plasmid with a 5-kbp DNA insert. The **galE**-complementing activity was localized to a 2.2-kbp DNA region by subcloning. Biochemical, immunological, and phage sensitivity analyses of the recombinant LPS in S. typhimurium showed that it is essentially identical to that of the wild type. In vivo expression studies showed that a 37-kDa protein is expressed from the complementing plasmids, and the presence of **GalE** activity was confirmed by an assay for epimerase activity. Nucleotide sequence analysis of the cloned DNA identified the **galE** gene. Comparison of the deduced amino acid sequence of P. haemolytica A1 **GalE** with published data showed high-level homology, 81.6%, with the **GalE** of Haemophilus influenzae **type b**. However, the sequences flanking **galE** do not show similarity with any other gal gene, suggesting that P. haemolytica A1 **galE** is not linked to the other genes of the gal operon, as is the case for **Neisseria meningitidis, Neisseria gonorrhoeae,** and H. influenzae. The separation of **galE** from the classical gal operon genes was confirmed by Southern blot hybridization studies, and a physical map showing the relative positions of **galE**, galT, and galK was constructed.

L25 ANSWER 15 OF 27 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 95:39500 DISSABS Order Number: AAIC423425 (not available for sale by UMI)
TITLE: AN INVESTIGATION INTO THE VIRULENCE COMPONENTS OF NEISSERIA MENINGITIDIS
AUTHOR: MACKINNON, FIONA GWYNNETH [D.PHIL.]
CORPORATE SOURCE: OPEN UNIVERSITY (UNITED KINGDOM) (0949)
SOURCE: Dissertation Abstracts International, (1994) Vol. 56, No. 3C, p. 626. Order No.: AAIC423425 (not available for sale by UMI).
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19950906
Last Updated on STN: 19950906

AB An animal infection model for meningococcal disease which involves intranasal infection of infant mice with 10$\sp8$ meningococci, was developed. The infection was followed by sampling bacteria from the nasal passages, lungs and blood for three days post-inoculation. The route of infection in mice proceeded from the nasal passages to the lungs and subsequently to blood infection. Exogenous iron in the form of iron dextran or human transferrin (administered intraperitoneally before and during infection) was required for meningococci to establish nasal colonisation and to disseminate to cause lung and blood infection.

An iron-uptake mutant of N. meningitidis, which was defective in the ability to utilise iron bound to human transferrin and lactoferrin was isolated. The infectivity of the mutant was found to be greatly reduced in mice when human transferrin was supplied as an exogenous iron source compared to iron dextran, compounding previous evidence that efficient iron-uptake is a pre-requisite for survival and proliferation in vivo. After further phenotypic characterisation, the mutant was found to be similar to E. coli TonB mutants, which have intact receptor function and over-express iron-regulated proteins but are unable to internalise specific nutrients, suggesting that the uptake of iron from transferrin and lactoferrin by N. meningitidis is analogous to the TonB transport system of specific nutrients by Enterobacteriaceae.

The mouse infection model was successfully used to differentiate the virulence of several B15 P1.7,16 **meningococcal** strains, isolated during a prolonged outbreak of **meningococcal** disease in Gloucestershire, and which varied with respect to: (1) whether they were isolated from a case of disease or from the nasopharynx of a carrier, (2) the level of **group B** capsule, and (3) **lipooligosaccharide** (**LOS**) immunotype (expressing either the L1,8,10 immunotype only, the L3,7,9 immunotype only, or both simultaneously). The possession of **group B** capsule appeared to be the most important factor for murine virulence, but expression of the L3,7,9 immunotype was also important as a secondary factor. Murine virulence of **meningococcal** strains was found to be related to the ability of the strains to survive in vitro in normal human serum. In **gonococci**, it has previously been shown that sialylation of **LOS** confers serum resistance to the cell. The target site for addition of sialic acid (defined by monoclonal **antibody** 3F11) was confirmed to be present on the L3,7,9 **LOS**

component, indicating that **meningococcal** strains expressing this immunotype were sialylatable. The relative contribution of both capsule and sialylation of **LOS** on serum resistance varied amongst **meningococcal** strains, with neither alone resulting in complete serum resistance, suggesting an interactive mechanism of the two.

During murine virulence studies, two atypical case strains (L91 1134 and L352), which initially expressed only the L1,8,10 (non-sialylatable) **LOS** immunotype, underwent phenotypic switching to also expressing the L3,7,9 (sialylatable) immunotype. This change was associated with increased murine virulence and increased serum resistance. On further investigation, populations of L91 1134 and L352 isolated from mice were found to consist of single cells possessing either the L1,8,10, the L3,7,9, or both **LOS** immunotypes together.

L25 ANSWER 16 OF 27 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 94274312 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7516313
TITLE: Tn916-generated, **lipooligosaccharide** mutants of Neisseria meningitidis and Neisseria **gonorrhoeae**.
AUTHOR: Stephens D S; McAllister C F; Zhou D; Lee F K; Apicella M A
CORPORATE SOURCE: Department of Medicine, Emory University School of Medicine, Atlanta, Georgia.
CONTRACT NUMBER: AI 18384 (NIAID)
AI 33517 (NIAID)
SOURCE: Infection and immunity, (1994 Jul) 62 (7) 2947-52.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940729
Last Updated on STN: 19960129
Entered Medline: 19940720

AB A library of Tn916-generated, tetracycline-resistant (Tc) mutants of the **group B Neisseri meningitidis** strain NMB was screened by using monoclonal **antibodies** (MAbs) that recognize structural differences in **neisserial lipooligosaccharide** (**LOS**). The **LOS** of parental strain NMB had a relative molecular mass of 4.5 kDa, reacted with MAbs 3F11 and 6B4 but not with MAb 4C4 or 6E4, and contained a lacto-N-neotetrose unit. Two phenotypically stable mutants, SS3 and R6, altered in **LOS**, were identified by colony immunoblots, electrophoresis, and Western immunoblots. The **LOS** of mutant SS3 was 3.4 kDa and reacted with MAbs 4C4 and 6E4 but not MAb 3E11 or 6B4. The **LOS** of mutant R6 was 3.1 to 3.2 kDa and reacted with MAb 6E4 but not MAb 3F11, 6B4, or 4C4. Thus, the LOSs of the R6 and SS3 mutants were predicted to contain different truncations of the core oligosaccharide. The **LOS** phenotype of each mutant was linked to Tc(r), as determined by transformation of the parent strain with DNA from the mutant. Southern hybridizations and

single-specific-primer PCR revealed in each mutant a single truncated tn916 insertion which had lost genes required for mobilization. Tn916 mutagenesis was used to identify two distinct genetic sites in the meningococcal chromosome involved in biosynthesis of the oligosaccharide chain of **LOS** and to create genetically defined **LOS** mutants of N. meningitidis and Neisseria **gonorrhoeae**.

L25 ANSWER 17 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 92135122 EMBASE
DOCUMENT NUMBER: 1992135122
TITLE: **Lipooligosaccharides** (**LOS**) of some Haemophilus species mimic human glycosphingolipids, and some **LOS** are sialylated.
AUTHOR: Mandrell R.E.; McLaughlin R.; Kwaik Y.A.; Lesse A.; Yamasaki R.; Gibson B.; Spinola S.M.; Apicella M.A.
CORPORATE SOURCE: Department of Medicine, State University of New York,Buffalo, NY 14215, United States
SOURCE: Infection and Immunity, (1992) 60/4 (1322-1328). ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The **lipooligosaccharides** (**LOS**) of strains of Haemophilus ducreyi, **Neisseria gonorrhoeae**, **Neisseria meningitidis**, and **Neisseria** lactamica contain epitopes that are antigenically and structurally similar to carbohydrates present in human glycosphingolipids. **LOS** from strains of Haemophilus influenzae and H. influenzae biogroup aegyptius were tested for the binding of monoclonal **antibodies** (MAbs) that bind to human glycosphingolipids possessing Galβ1-4GlcNAc (MAb 3F11) and Galα1-4Galβ1-4Glc (MAb anti-P(k)). In solid-phase radioimmunoassays, the **LOS** of 18 of 19 H. influenzae **type b** (Hib), 8 of 19 nontypeable H. influenzae, and 10 of 20 H. influenzae biogroup aegyptius strains bound MAb anti-P(k). The **LOS** of 13 of 19 Hib, 10 of 16 nontypeable H. influenzae, and 2 of 18 H. influenzae biogroup aegyptius strains bound MAb 3F11. Neuraminidase treatment of the strains increased the binding of MAb 3F11 by more than twofold in 47% of the H. influenzae strains, suggesting that sialic acid occluded the **LOS** structure recognized by MAb 3F11. The material released from neuraminidase-treated Hib **LOS** was confirmed to be sialic acid by high-performance anion-exchange chromatography. A recombinant plasmid containing genes involved in Hib **LOS** biosynthesis directed the expression (assembly) of the 3F11 epitope in Escherichia coli. These studies demonstrate that H. influenzae and H. influenzae biogroup aegyptius express at least two **LOS** epitopes that are similar to those present in human glycosphingolipids. Sialic acid was present on the **LOS** of some H. influenzae strains and

prevented the binding of MAb 3F11 to its epitope. The oligosaccharide portion of sialylated **LOS** may also resemble sialylated oligosaccharides present in human glycosphingolipids (gangliosides).

L25 ANSWER 18 OF 27 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 91210172 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1708379
TITLE: Endogenous sialylation of the **lipooligosaccharides** of Neisseria meningitidis.
AUTHOR: Mandrell R E; Kim J J; John C M; Gibson B W; Sugai J V; Apicella M A; Griffiss J M; Yamasaki R
CORPORATE SOURCE: Center for Immunochemistry, Veterans Administration Medical Center, San Francisco, California 94121.
CONTRACT NUMBER: AI 18384 (NIAID)
AI 21620 (NIAID)
AI 28871 (NIAID)
+
SOURCE: Journal of bacteriology, (1991 May) 173 (9) 2823-32.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910616
Last Updated on STN: 19970203
Entered Medline: 19910530

AB Monoclonal **antibodies** (MAb) 3F11 and 06B4 recognize epitopes that are conserved on **gonococcal lipooligosaccharides** (**LOS**), present on some meningococcal **LOS**, and conserved on human erythrocytes. **LOS** of some **group B** and C prototype **meningococcal LOS** strains (**LOS** serotypes L1 to L8) treated with neuraminidase showed increased expression of the 3F11 and 06B4 MAb-defined epitopes. Neuraminidase-treated **LOS** separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and silver stained showed a shift in migration from a component with a mass of approximately 4.8 kDa to a component with a mass of between 4.5 and 4.6 kDa. The same strains grown in medium with excess CMP-N-acetylneuraminic acid had **LOS** that shifted in migration to a slightly higher component (mass, approximately 4.8 kDa). Chemical analysis of the neuraminidase-digested products from one **LOS** indicated it contained approximately 1.5% sialic acid. Covalent linkage between sialic acid and the **LOS** was confirmed by analysis of de-O-acylated and dephosphorylated **LOS** by liquid secondary ion mass spectrometry. Three studies show that some meningococci contain sialic acid in their **LOS**, that the sialic acid is cleaved and lost in conventional acetic acid hydrolysis, and that the sialic acid alters the expression of MAb-defined epitopes.

L25 ANSWER 19 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1989-033857 [05] WPIDS
DOC. NO. CPI: C1989-014704

TITLE: Vaccine against **gp. B** **Neisseria meningitidis** - containing high mol. weight protein antigenic complex, vesicles and a capsular polysaccharide component.

DERWENT CLASS: B04 C03 D16

INVENTOR(S): DOMINGUEZ, M A G; GONZALEZ, V G S; HERRERA, M D C S; HUERGO, C C; IMIA, L G G; JORRIN, G B; MORALES, E X L R; PADRON, F S; RIZO, G D L C P; VAZQUEZ, M M G; HERRERA, M D C; MORALES, E X L; RIZO, G D L; MORALES, E Z L R; BISSET JORRIN, G; CAMPA HUERGO, C; GALGUERA DOMINGUEZ, M A; GARCIA IMIA, L G; GUTIERREZ VAZQUEZ, M M; PUENTES RIZO, G D L C; SAMPEDRO HERRERA, M D C; SIERRA GONZALEZ, V G; SOTOLONGO PADRON, F; XOCHITL LE RIVEREND MORALES, E; BISSETJORR, G; CAMPAHUERG, C; GARCIAIMIA, L G; GUTIERREZV, M M; PUENTESRIZ, G D L; SAMPEDROHE, M D C; SIERRAGONZ, V G; SOTOLONGOP, F; PUENTES RIZO, G; SAMPEDRO HERRERA, M; DE LA CARIDAD PUENTES RIZO, G; DEL CARMEN SAMPEDRO, M; GALGUERA, M A; GONZALES, V G S; LE RIVEREND MORALES, E X; DEL CARMEN SAMPEDRO HERRERA, M; VAZCUEZ, M M G

PATENT ASSIGNEE(S): (NABI-N) CENT NACIONAL BIOPREPARADOS; (FINL-N) INST FINLAY

COUNTRY COUNT: 19

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 301992	A	19890201	(198905)*	EN	12
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
JP 01125328	A	19890517	(198926)		
AU 8820312	A	19890525	(198929)		
NO 8803647	A	19900312	(199016)#		
AU 9181349	A	19911031	(199151)		
AU 9453197	A	19940324	(199417)		
EP 301992	B1	19950524	(199525)	EN	18
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
RU 2023448	C1	19941130	(199527)		11
DE 3853854	G	19950629	(199531)		
ES 2074445	T3	19950916	(199543)		
NO 179998	B	19961021	(199648)#		
US 5597572	A	19970128	(199710)		9
AU 9674226	A	19970220	(199716)		
US 5747653	A	19980505	(199825)		
AU 706213	B	19990610	(199934)		
CA 1341199	C	20010306	(200116)	EN	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 301992	A	EP 1988-500077	19880730
JP 01125328	A	JP 1988-190500	19880729
AU 9453197	A	AU 1994-53197	19940114
	Div ex	AU 1991-81349	
EP 301992	B1	EP 1988-500077	19880730

Searcher : Shears 571-272-2528

RU 2023448	C1		SU 1988-4356456	19880729
DE 3853854	G		DE 1988-3853854	19880730
			EP 1988-500077	19880730
ES 2074445	T3		EP 1988-500077	19880730
NO 179998	B		NO 1988-3647	19880816
US 5597572	A	Cont of	US 1988-225859	19880729
		Cont of	US 1991-767341	19910927
			US 1993-152938	19931112
AU 9674226	A	Div ex	AU 1994-53197	19940114
			AU 1996-74226	19961206
US 5747653	A	Cont of	US 1988-225859	19880729
		Cont of	US 1991-767341	19910927
		Div ex	US 1993-152938	19931112
			US 1996-692055	19960802
AU 706213	B	Div ex	AU 1994-53197	19940114
			AU 1996-74226	19961206
CA 1341199	C		CA 1988-573538	19880801

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3853854	G	Based on	EP 301992
ES 2074445	T3	Based on	EP 301992
NO 179998	B	Previous Publ.	NO 8803647
US 5747653	A	Div ex	US 5597572
AU 706213	B	Previous Publ.	AU 9674226

PRIORITY APPLN. INFO: CU 1987-125 19870730

AN 1989-033857 [05] WPIDS

AB EP 301992 A UPAB: 19950712

A vaccine with wide long-lasting protective range against different **pathogenic serotypes** of **gp. B Neisseria meningitidis** is claimed which contains an immunologically effective quantity of the protein antigenic complex of 65-95 kD mol. weight, that confers antigenic immunity in the presence of different known **pathogenic** serotypes and induces the formation of bactericidal **antibodies**, a quantity of vesicles in the necessary proportions that induces a strong response of specific **antibodies** to the antigenic serotype determinants and to the **endotoxin**, and a capsular polysaccharide proportion that increases solubility and immunogenicity of the whole, which also increases the response to the polysaccharide component, even in children under 2 years of age and defines its polyvalent property and whose preparation is optimised by the necessary quantity of adjuvant.

USE - The prods. are used for prophylaxis and treatment of diseases caused by **gp. B Neisseria meningitidis.**

0/1

Dwg.0/1

ABEQ EP 301992 B UPAB: 19950630

Method for obtaining a vaccine against the different **pathogenic serotypes** of **group B Neisseria meningitidis** characterised by starting from live microorganisms of any one of the known **pathogenic**

serotypes of the **group B** without inactivation,
from which the extraction of the vesicles of the outer membrane and the protein antigenic complex of 65-95 KD molecular weight is carried out using detergent, lysozyme and ultrasound combined in the treatment, the resulting product, after treatment to eliminate the nucleic acids, is purified by a dissociating treatment with detergent, ultrasonic bath and column chromatography, the multi antigenic-material so obtained is purified to obtain the protein antigenic complex of 65-95 KD molecular weight for HPLC chromatography using a column such as TSK 3000 SWG(R), or affinity chromatography with monoclonal **antibodies**, or hydrophobic interaction chromatography, or ionic exchange chromatography or a combination of any one of them, the protein antigenic complex is added to the fraction that contains the vesicles by ultrasound treatment so that it will be nachored on them, in a proportion of 15 per cent +/- 3, the capsular polysaccharide is also added, in a portion of 1:1-1:4 with respect to the protein and the adjuvant in a relation ranging from 20-100 ug/protein ug, the different components of the mixture may be sterilised by cobalt 60 ionizing radiations with doses from 5-25 Kgy and a temperature between 1-4 deg.C before preparing the mixture, or the resulting mixture may be sterilised by this procedure.
Dwg.0/0

ABEQ US 5597572 A UPAB: 19970307
A method for producing a vaccine against **Neisseria** meningitidis B **pathogens** comprising the steps performed in the following order of:

a) extracting the vesicles of the outer membrane and protein antigenic complex weighing from 65 to 95 kD from live, active pathogens of group B serotypes with a treatment selected from the group consisting of:

(i) treating with detergent,

(ii) treating with detergent and ultrasound, and

(iii) treating with detergent, enzymatic solution and ultrasound to create an extract;

b) treating said extract to eliminate nucleic acids to create a treated extract;

c) purifying said treated extract to separate as a fraction the said vesicles from the protein antigenic complex by a dissociative treatment with detergent solution, ultrasound, and column chromatography to produce purified protein antigenic complex;

d) further purifying said purified protein antigenic complex by a chromatographic step from the group consisting of high performance liquid chromatography, affinity chromatography with monoclonal **antibodies**, hydrophobic chromatography, and ionic exchange chromatography, and combinations thereof, to obtain a further purified protein antigenic complex;

e) combining said further purified protein antigenic complex with a fraction containing the vesicles by ultrasound treatment to anchor said further purified protein antigenic complex and vesicles to each other in an effective mount in a proportion of 15% plus or minus 3% by weight to create an anchored protein complex; and,

f) adding capsular polysaccharide and adjuvant to anchored protein complex of step (e), wherein the adjuvant is selected from the group consisting of aluminum hydroxide, aluminum phosphate, and calcium phosphate; and recovering the resultant vaccine.

Dwg.0/1

L25 ANSWER 20 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 89046389 EMBASE
DOCUMENT NUMBER: 1989046389
TITLE: Neisseria lactamica and Neisseria meningitidis share **lipooligosaccharide** epitopes but lack common capsular and class 1, 2, and 3 protein epitopes.
AUTHOR: Kim J.J.; Mandrell R.E.; Griffiss J.M.
CORPORATE SOURCE: Centre for Immunochemistry, University of California, San Francisco, CA 94143, United States
SOURCE: Infection and Immunity, (1989) 57/2 (602-608). ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Neisseria** lactamica, a common human pharyngeal commensal, contributes to acquired immunity to **Neisseria meningitidis**. To define the surface antigens shared between these two species, we used monoclonal **antibodies** (MAbs) to study 35 N. lactamica strains isolated in various parts of the world for cross-reactivity with **meningococcal** capsules, outer membrane proteins, and **lipooligosaccharides** (**LOS**). No N. lactamica strain reacted significantly with MAbs specific for capsular **group** A, **B**, C, Y, or W, and we were unable to extract capsular polysaccharide from them. Only 2 of 33 strains reacted weakly with MAbs against class 2 serotype proteins P2b and P2c. None reacted with MAbs specific for **meningococcal** class 1 protein P1.2 or P1.16 or class 2/3 serotype protein P2a or P15. Most N. lactamica strains (30 of 35) bound one or more of seven **LOS**-specific MAbs. Two **LOS** epitopes, defined by MAbs O6B4 and 3F11, that are commonly found on **pathogenic Neisseria** species were found on 25 of 35 N. lactamica. Analysis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and immunoblotting showed that the **LOS** of N. lactamica are composed of multiple components that are physically and antigenically similar to the **LOS** of **pathogenic Neisseria** species. Among four other commensal **neisserial** species, only **Neisseria** cinerea shared **LOS** epitopes defined by MAbs O6B4 and 3F11. Previous studies have shown that pharyngeal colonization with N. lactamica induces bactericidal **antibodies** against the **meningococcus**. We postulate that shared N. lactamica and **meningococcal LOS** epitopes may play an important role in the development of natural immunity to the **meningococcus**.

L25 ANSWER 21 OF 27 MEDLINE on STN
ACCESSION NUMBER: 88129035 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3124365
TITLE: Synergistic effect of detergents and aluminium phosphate on the humoral immune response to bacterial

and viral membrane proteins.
AUTHOR: Teerlink T; Beuvery E C; Evenberg D; van Wezel T L
CORPORATE SOURCE: Department of Bacterial Vaccines, National Institute of Public Health and Environmental Hygiene (RIVM), Bilthoven, The Netherlands.
SOURCE: Vaccine, (1987 Dec) 5 (4) 307-14.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880229

AB The influence of detergents on the immunogenic activity of the major outer membrane protein of Neisseria **gonorrhoeae** was investigated. Most detergents tested were found to enhance the immune response. This effect was synergistic with the adjuvant activity of AlPO4. The combination of detergent and AlPO4 showed a stronger adjuvant activity than Freund's complete adjuvant. The adjuvant effect was only observed with protein preparations with very low **lipopolysaccharide** content. The immunostimulating effect of detergents was also observed with **meningococcal** group C polysaccharide conjugated to a Haemophilus influenzae **type b** outer membrane protein and with the fusion protein of measles virus. The influence of some detergent parameters (critical micelle concentration, hydrophile-lipophile balance, charge) was investigated.

L25 ANSWER 22 OF 27 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 86141984 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3081658
TITLE: Definition of a virulence-related antigen of Neisseria **gonorrhoeae** with monoclonal **antibodies** and lectins.
AUTHOR: Demarco de Hormaeche R; Bundell C; Chong H; Taylor D W; Wildy P
SOURCE: Journal of infectious diseases, (1986 Mar) 153 (3) 535-46.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198604
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860402

AB Variants of one strain of Neisseria **gonorrhoeae**, grown in vivo or in vitro, that have been previously shown to differ in infectivity, serum resistance, and capsule production were compared with use of monoclonal **antibodies** and lectins. Monoclonal **antibodies** to virulent **gonococci** recognized an antigenic site of the **lipopolysaccharide** (**LPS**) produced in large amounts by **gonococci** grown in vivo but

present only in a small proportion of in vitro-grown **gonococci**. This antigen (C-**LPS**) was found in all 85 different **gonococcal** isolates studied but not among nonpathogenic neisseriae. It was shared by **group B** and C **meningococci** but not by groups A and D. Enzyme-linked immunosorbent assay and Western blot analysis showed that N-acetylglucosamine and N-acetylgalactosamine form part of the epitope. The C-**LPS** antigen was shown by immunofluorescence to be present on the surface of the **gonococci** and also free as slime. This antigen appears to confer resistance to killing by normal sera.

L25 ANSWER 23 OF 27 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 85093533 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6440412
TITLE: Affinity chromatography for purification of **antibodies** to Neisseria **gonorrhoeae** and Neisseria meningitidis **lipopolysaccharides**.
AUTHOR: Rodahl E; Maeland J A
SOURCE: Acta pathologica, microbiologica, et immunologica Scandinavica. Section C, Immunology, (1984 Oct) 92 (5) 247-54.
Journal code: 8206624. ISSN: 0108-0202.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198502
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850221

AB **Lipopolysaccharides** (LPSs) were prepared by phenol-water extraction of the **gonococcal** strain 8551 and the **group B meningococcal** strain 44/76, digested with pronase, and purified by ultracentrifugation and Sepharose CL-6B fractionation in the presence of 1.5 per cent sodium deoxycholate. On SDS-PAGE with 10 per cent acrylamide the purified 125I-labelled LPSs migrated as single, low-molecular-weight components. The LPSs were coupled to CNBr-activated Sepharose 4B for affinity purification of **antibodies** to the common antigenic factor 1 and the sero-type factor 5 of **LPS** 8551, and **antibodies** to **LPS** 44/76. The **antibodies** eluted showed ELISA activity against wells coated with **LPS** or whole cells of the bacteria, the **antibody** activity being inhibited by **LPS**. SDS-PAGE of whole cells of the strain 8551 and immunoblotting with the anti-factor 1 or -factor 5 **antibodies** resulted in single, broad bands corresponding to the low-molecular-weight **LPS** subunits.

L25 ANSWER 24 OF 27 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 84136236 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6142055
TITLE: Enzyme-linked immunosorbent assay with a monoclonal **antibody** for detecting group A meningococcal

antigens in cerebrospinal fluid.
AUTHOR: Sugasawara R J; Prato C M; Sippel J E
SOURCE: Journal of clinical microbiology, (1984 Feb) 19 (2) 230-4.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198404
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19950206
Entered Medline: 19840425

AB Hybridomas were produced from spleen cells of BALB/c mice immunized with a membrane preparation from Neisseria meningitidis group A strain 4402 and S194/5.XXOBU.14 myeloma cells. The hybridomas were screened for secretion of **antibodies** suitable for an enzyme-linked immunosorbent assay (ELISA) diagnostic for group A meningococcal meningitis. One hybridoma **antibody**, 3G7, was directed against the pilus protein. This **antibody** bound to all six **lipopolysaccharide** and protein group A **meningococcal** serotyping strains, as well as to **meningococcal** strains from serogroups C, W135, and Y, but not to a strain of Escherichia coli, Haemophilus influenzae **type b**, or to two or more strains of Streptococcus pneumoniae, **Neisseria gonorrhoeae**, and Salmonella typhi. The ELISA used on **antibody**, antigen, **antibody**-conjugate sandwich. Rabbit anti-meningococcal serum was the coating **antibody** for the **antibody** sandwich, cerebrospinal fluids contained the bacterial antigens, and 3G7-alkaline phosphatase conjugate was the detecting **antibody**. The monoclonal **antibody** conjugate ELISA system was able to detect group A meningococcal antigens in 21 of 25 cerebrospinal fluid specimens that were positive in an immune rabbit serum conjugate ELISA; cerebrospinal fluid samples from patients with Haemophilus meningitis served as the controls. Counterimmunoelectrophoresis detected meningococcal antigens in 16 of the same 25 cerebrospinal fluid samples.

L25 ANSWER 25 OF 27 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 84060229 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6417025
TITLE: Monoclonal **antibodies** against Neisseria meningitidis **lipopolysaccharide**.
AUTHOR: Sugasawara R J; Prato C; Sippel J E
SOURCE: Infection and immunity, (1983 Dec) 42 (3) 863-8.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198401
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19840107

AB A cell line producing monoclonal **antibodies** directed

against a **lipopolysaccharide** component of Neisseria meningitidis group A has been established. These **antibodies** reacted with only one of three **lipopolysaccharide** serotyping strains of group A meningococci by coagglutination, enzyme-linked immunosorbent assay, and Western blotting techniques. A Western blot analysis showed that a NaOH digest of **lipopolysaccharide** was detectable by the serotype-specific **antibody**. The monoclonal **antibodies** cross-reacted with a **group B meningococcal** strain in an enzyme-linked immunosorbent assay. The immunoblotting analysis also showed that these **antibodies** reacted with the **lipopolysaccharides** of a **group B meningococcus** as well as Haemophilus influenzae **type B**, but not with the **lipopolysaccharides** of several strains of Salmonella typhi, Escherichia coli, Streptococcus pneumoniae, and **Neisseria gonorrhoeae.**

L25 ANSWER 26 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 75118374 EMBASE
DOCUMENT NUMBER: 1975118374
TITLE: Protein fraction with immunogenic potential and low toxicity isolated from the cell wall of **Neisseria meningitidis group B.**
AUTHOR: Hill J.C.; Weiss E.
CORPORATE SOURCE: Dept. Microbiol., Nav. Med. Res. Inst., Bethesda, Md. 20014, United States
SOURCE: Infection and Immunity, (1974) 10/3 (605-615). CODEN: INFIBR
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
004 Microbiology
LANGUAGE: English

AB Several fractions were extracted from the cell envelope (CE) of N. **meningitidis group B** and characterized with regard to their morphology, antigenicity, protein composition, and toxicity. Whole bacterial cells were suspended in a medium of low ionic strength and disrupted in a French pressure cell. The crude CE thus obtained were separated into cell membrane (CM) enriched and cell wall (CW) enriched fractions on sucrose density gradients. In addition, CM and CW fractions were separated from CE on the basis of differential solubility in the nonionic detergent, Triton X 100. The Triton insoluble fraction, containing primarily CW components, was further treated with a mixture of Triton and ethylenediaminetetraacetic acid, which was shown to remove additional protein and most of the **lipopolysaccharide.** Electron microscope examination of the various fractions revealed typical unit membrane structures in the case of CM, or large, open segments in the case of CW. The Triton insoluble and especially the Triton ethylenediaminetetraacetic acid insoluble fractions consisted of small vesicular structures. All fractions, except the Triton soluble fraction, when assayed by sodium dodecyl sulfate polyacrylamide gel electrophoresis, were shown to contain one major protein component accounting for more than 50% of the total. Sera from rabbits immunized with the various fractions formed precipitin

lines in immunodiffusion tests against the homologous and some of the heterologous fractions. High titer bactericidal **antibodies** were also demonstrated in these sera when tested against the homologous strains. Toxicity studies in rats sensitized with lead acetate indicate that the level of contamination of Triton insoluble/Triton ethylenediaminetetraacetic acid insoluble fractions with **lipopolysaccharide** was significantly smaller than that of the other fractions.

L25 ANSWER 27 OF 27 FEDRIP COPYRIGHT 2004 NTIS on STN
ACCESSION NUMBER: 2004:181826 FEDRIP
NUMBER OF REPORT: CRISP 1Z01HD01301-19
RESEARCH TITLE: Immune Response To Polysaccharide-protein Conjugate Vacc
STAFF: Principal Investigator: SCHNEERSON, RACHEL
SUPPORTING ORGN: Supported By: NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
FISCAL YEAR: 2001
FUNDING: Not Applicable
FILE SEGMENT: National Institutes of Health
SUM Surface polysaccharides of **pathogenic** bacteria, including capsular polysaccharides (CPS) or **lipopolysaccharides** (**LPS**), serve both as essential virulence factors and as protective antigens. The age-related and T-cell independent immunogenicity of CPS limit their use as vaccines especially in infants and young children. **LPS** are too toxic to be administered. Accordingly, their O-specific polysaccharide (O-SP), that share the virulence promoting and protectiveness of CPS, must be purified: O-SP are too small to be immunogenic (haptens). Covalent binding of CPS or of O-SP to medically-useful proteins to form conjugates both increases their immunogenicity and confers T-cell dependence to these saccharides. The O-SP of Shigella sonnei and of Shigella flexneri 2a were bound to bacterial toxoids. In adults and then in 4-7 year-olds, both conjugates were safe and induced statistically significant and long-lived rises of IgG **antibodies** to the homologous **LPS**. Similar, though lesser rises of IgM and IgA anti-**LPS** were also induced. Re-injection of S. flexneri 2a conjugate induced a booster response in the recruits and the 4-7 years old. A Phase 3 trial showed that one injection of S. sonnei O-SP, bound to a non-toxic recombinant Pseudomonas aeruginosa exoprotein A (rEPA) protected army recruits against outbreaks with this **pathogen**. Importantly, there was a statistically-significant correlation between the levels of serum IgG anti-**LPS** and the efficacy of the conjugate. Two methods were developed that increased the immunogenicity of the Shigella conjugates in mice: another carrier protein, a genetically-inactivated Corynebacterium diphtheriae toxin (CRM9) was a superior carrier for S. sonnei O-SP and treatment of rEPA with succinic anhydride, a non-toxic mild akylating agent that converts amino groups of proteins to carboxyls, increased the immunogenicity of S. flexneri 2a O-SP. A phase 1 study in adults of these Shigella conjugates confirmed their safety and immunogenicity; the improved immunogenicity was less marked than in mice. A phase 2 study in 1-4 years old showed an improved immunogenicity of the new S.flexneri 2a conjugate but lesser immunogenicity of the S.sonnei conjugate. A phase 3 study of the modified S.flexneri 2a and the original S.

sonnei conjugates are in preparation. In collaboration with the Lanzhou Vaccine Institute and Provincial Medical Center in Henan, China, a clinical trial of these two conjugates is being planned. To investigate if concurrent administration of a cross-reacting along with a homologous CPS has an advantage over the use of the homologous CPS alone, the cell wall polysaccharide (PS) of Bacillus pumilus, SH18, reported to cross react with the CPS of haemophilus influenzae **type b** (Hib), was isolated by conventional methods and it?s structure investigated using GC-MS. It was shown to contain glycerol, ribitol and 2-acetamido-2-deoxyglucose in a molar ratio of 0.2:1.0:0.2 and 17% phosphate. Besides with the anti Hib it cross reacted with anti Staphilococcus epidermidis. Methods to prepare a conjugate of this PS are investigated. **Neisseria meningitidis** group A causes endemic and epidemic meningitis, notably in the meningitis belt of Africa. A CPS vaccine , effective and available, is underutilized. To further improve it?s immunogenicity, as was done for other CPS, methods of binding it to a carrier protein are being investigated. A double mutant of Bordetella pertussis, producing a genetically-inactivated toxin and deficient in FHA synthesis was developed. Effort is directed towards increasing production of this B. pertussis strain as a more easily purified pertussis toxin for a monocomponent vaccine and as a carrier protein for pneumococcal type 14 CPS. Clostridium difficile is a major cause of hospital-acquired diarrhea following antibiotic usage: the diarrhea is mediated by two exotoxins, A and B. Toxin A, considered to be the major toxin, in the extreme form will cause pseudomembranous colitis. A genetically-derived toxin mutant (rARU) induces both antitoxin and protects animals from infection with C. difficile. The succinylation of rARU improved its solubility and did not detectably affects its antigenicity. Techniques to prepare the mutant toxins A for clinical use have been worked out. Three polysaccharide of varying composition, pneumococcus type 14, Escherichia coli K1 and S. flexneri 2a were conjugated to succinylated rARU. The resultant conjugates induced high levels of both anti-polysaccharide and antitoxin. Preparation of toxin A conjugates for clinical evaluation is underway. Borrelia burgdorferi, a spirochete transmitted though the bite of infected Ixodes ticks, is the etiologic agent of Lyme disease. A protein vaccine against it is available but is not effective below the age of 12 years. **LPS** has been described in other spirochetes but it's presence in B. burgdorferi has been debated. So far we have not been able to confirm it's presence. The search for **LPS** revealed a unique glycolipid cosisting of glycerol and galactose as the carbohydrate moiety. There is evidence that this glycolipid is surface exposed Injected in complete Freund's adjuvant it induced specific **antibodies** .

FILE 'MEDLINE' ENTERED AT 15:52:01 ON 14 JUL 2004

L26	39	SEA FILE=MEDLINE ABB=ON PLU=ON "NEISSERIA MENINGITIDIS, SEROGROUP B"/CT
L27	6276	SEA FILE=MEDLINE ABB=ON PLU=ON "NEISSERIA GONORRHOEAE"/CT
L28	0	SEA FILE=MEDLINE ABB=ON PLU=ON L26 AND L27

Searcher : Shears 571-272-2528

L26	39	SEA FILE=MEDLINE ABB=ON	PLU=ON	"NEISSERIA MENINGITIDIS, SEROGROUP B"/CT
L29	6700	SEA FILE=MEDLINE ABB=ON	PLU=ON	VACCINES/CT
L30	32958	SEA FILE=MEDLINE ABB=ON	PLU=ON	IMMUNIZATION/CT
L31	5	SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND (L29 OR L30)

L26	39	SEA FILE=MEDLINE ABB=ON	PLU=ON	"NEISSERIA MENINGITIDIS, SEROGROUP B"/CT
L32	33840	SEA FILE=MEDLINE ABB=ON	PLU=ON	LIPOPOLYSACCHARIDES/CT
L33	17012	SEA FILE=MEDLINE ABB=ON	PLU=ON	ENDOTOXINS/CT
L34	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	L26 AND (L32 OR L33)

L35 6 L31 OR L34

L35 ANSWER 1 OF 6 MEDLINE on STN

ACCESSION NUMBER: 2004146179 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15039331
TITLE: Vaccine potential of the Neisseria meningitidis 2086 lipoprotein.
AUTHOR: Fletcher Leah D; Bernfield Liesel; Barniak Vicki; Farley John E; Howell Alan; Knauf Melissa; Ooi Peggy; Smith Robert P; Weise Paige; Wetherell Mike; Xie Xiaoling; Zagursky Robert; Zhang Ying; Zlotnick Gary W
CORPORATE SOURCE: Wyeth Vaccines Research, Pearl River, New York 10965, USA.
SOURCE: Infection and immunity, (2004 Apr) 72 (4) 2088-100. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY330352; GENBANK-AY330353; GENBANK-AY330354; GENBANK-AY330355; GENBANK-AY330356; GENBANK-AY330357; GENBANK-AY330358; GENBANK-AY330359; GENBANK-AY330360; GENBANK-AY330361; GENBANK-AY330362; GENBANK-AY330363; GENBANK-AY330364; GENBANK-AY330365; GENBANK-AY330366; GENBANK-AY330367; GENBANK-AY330368; GENBANK-AY330369; GENBANK-AY330370; GENBANK-AY330371; GENBANK-AY330372; GENBANK-AY330373; GENBANK-AY330374; GENBANK-AY330375; GENBANK-AY330376; GENBANK-AY330377; GENBANK-AY330378; GENBANK-AY330379; GENBANK-AY330380; GENBANK-AY330381; GENBANK-AY330382; GENBANK-AY330383; GENBANK-AY330384; GENBANK-AY330385; GENBANK-AY330386; GENBANK-AY330387; GENBANK-AY330388; GENBANK-AY330389; GENBANK-AY330390; GENBANK-AY330391; GENBANK-AY330392; GENBANK-AY330393; GENBANK-AY330394; GENBANK-AY330395; GENBANK-AY330396; GENBANK-AY330397; GENBANK-AY330398; GENBANK-AY330399; GENBANK-AY330400; GENBANK-AY330401; GENBANK-AY330402; GENBANK-AY330403; GENBANK-AY330404; GENBANK-AY330405; GENBANK-AY330406; GENBANK-AY330407; GENBANK-AY330408; GENBANK-AY330409; GENBANK-AY330410; GENBANK-AY330411; GENBANK-AY330412; GENBANK-AY330413; GENBANK-AY330414; GENBANK-AY330415

Searcher : Shears 571-272-2528

ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040325
Last Updated on STN: 20040510
Entered Medline: 20040507

ED Entered STN: 20040325
Last Updated on STN: 20040510
Entered Medline: 20040507

AB A novel antigen that induces cross-reactive bactericidal antibodies against a number of Neisseria meningitidis strains is described. This antigen, a approximately 28-kDa lipoprotein called LP2086, was first observed within a complex mixture of soluble outer membrane proteins (sOMPs) following a series of fractionation, protein purification, and proteomics steps. Approximately 95 different neisserial isolates tested positive by Western blotting and PCR screening methods for the presence of the protein and the gene encoding LP2086. The strains tested included isolates of N. meningitidis serogroups A, B, C, W135, and Y, Neisseria gonorrhoeae, and Neisseria lactamica. To better understand the microheterogeneity of this protein, the 2086 genes from 63 neisserial isolates were sequenced. Two different subfamilies of LP2086 were identified based on deduced amino acid sequence homology. A high degree of amino acid sequence similarity exists within each 2086 subfamily. The highest degree of genetic diversity was seen between the two subfamilies which share approximately 60 to 75% homology at the nucleic acid level. Flow cytometry (fluorescence-activated cell sorting) analyses and electron microscopy indicated that the LP2086 is localized on the outer surface of N. meningitidis. Antiserum produced against a single protein variant was capable of eliciting bactericidal activity against strains expressing different serosubtype antigens. Combining one recombinant lipidated 2086 (rLP2086) variant from each subfamily with two rPorA variants elicited bactericidal activity against all strains tested. The rLP2086 family of antigens are candidates worthy of further vaccine development.

L35 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2004114783 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15003635
TITLE: Clinical evaluation of a group B meningococcal N-propionylated polysaccharide conjugate vaccine in adult, male volunteers.
AUTHOR: Bruge Joelle; Bouveret-Le Cam Nancy; Danve Bernard; Rougon Genevieve; Schulz Dominique
CORPORATE SOURCE: Aventis Pasteur France, 1541 Avenue Marcel Merieux, 69280 Marcy-l'Etoile, France.. joelle.bruge@aventis.com
SOURCE: Vaccine, (2004 Mar 12) 22 (9-10) 1087-96. Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20040309

Searcher : Shears 571-272-2528

Last Updated on STN: 20040430
Entered Medline: 20040429

ED Entered STN: 20040309
Last Updated on STN: 20040430
Entered Medline: 20040429

AB The safety and immunogenicity of a group B meningococcal vaccine, consisting of N-propionylated (NPr) B capsular polysaccharide conjugated to tetanus toxoid, was tested for the first time, in 17 healthy male volunteers aged between 18 and 40 years. Four escalating dosages of vaccine were tested and each was given as three intramuscular injections at 4-week intervals. The vaccine was well tolerated and induced only mild and transient, dose-dependent, injection-site reactions. One month after the last injection, there was no evidence of the production of autoantibodies or antibodies binding to PSA-NCAM. The vaccine induced an increase in the pre-existing titres of IgM specific to B polysaccharide and NPr B polysaccharide. Moreover, it induced IgG antibodies specific to NPr B polysaccharide, which were undetectable before vaccination. However, no functional activity of vaccine-induced antibodies was demonstrated in bactericidal assays, opsonophagocytic tests or passive protection tests.

L35 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2004000602 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14688137
TITLE: Development, characterization, and functional activity of a panel of specific monoclonal antibodies to inner core lipopolysaccharide epitopes in Neisseria meningitidis.
AUTHOR: Gidney Margaret Anne J; Plested Joyce S; Lacelle Suzanne; Coull Philip A; Wright J Claire; Makepeace Katherine; Brisson Jean-Robert; Cox Andrew D; Moxon E Richard; Richards James C
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council, Ottawa, ON, K1A OR6, Canada.. margaretanne.gidney@nrc-cnrc.gc.ca
SOURCE: Infection and immunity, (2004 Jan) 72 (1) 559-69. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040103
Last Updated on STN: 20040203
Entered Medline: 20040202

ED Entered STN: 20040103
Last Updated on STN: 20040203
Entered Medline: 20040202

AB A panel of six murine monoclonal antibodies (MAbs) recognizing inner core lipopolysaccharide (LPS) epitopes of Neisseria meningitidis was prepared and characterized in order to determine the diversity of inner core LPS glycoforms among disease and carrier isolates. Two of these MAbs, L2-16 (immunoglobulin G2b [IgG2b]) and LPT3-1 (IgG2a), together with a third, previously described MAb, L3B5 (IgG3), showed reactivity, either individually or in combination,

with all except 3 of 143 disease and carriage isolates (125 of 126 strains from blood, cerebrospinal fluid, or skin biopsy samples and 15 of 17 from nasopharyngeal cultures). MAbs L3B5, L2-16, and LPT3-1 were further characterized in an indirect immunofluorescence assay. All three MAbs bound to the bacterial cell surface, findings that correlated strongly with whole-cell enzyme-linked immunosorbent assay and immunodot blots. However, in contrast to our findings with L3B5, cell surface binding of L2-16 or LPT 3-1 did not correlate with functional activity as determined by bactericidal or infant rat passive protection assays against wild-type N. meningitidis strains. These findings are provocative with respect to the requirements for protective activity of antibodies and the development of inner core LPS vaccines against invasive meningococcal disease.

L35 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2003150231 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12654800
TITLE: Development and evaluation of an improved mouse model of meningococcal colonization.
AUTHOR: Yi Kyungcheol; Stephens David S; Stojiljkovic Igor
CORPORATE SOURCE: Department of Microbiology and Immunology, Emory University School of Medicine, 1510 Clifton Road NE, Atlanta, GA 30322, USA.. kyi@emory.edu
CONTRACT NUMBER: AI 472870-01A1 (NIAID)
SOURCE: Infection and immunity, (2003 Apr) 71 (4) 1849-55. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: (EVALUATION STUDIES) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030402
Last Updated on STN: 20030513
Entered Medline: 20030512

ED Entered STN: 20030402
Last Updated on STN: 20030513
Entered Medline: 20030512

AB Studies of meningococcal pathogenesis have been severely restricted due to the absence of an adequate animal model. Given the significance of iron in meningococcal pathogenesis, we developed a model of Neisseria meningitidis colonization in outbred adult mice that included daily administration of iron dextran. While receiving iron, the animals were inoculated intranasally with the initial doses of bacterial suspension. Meningococci were recovered from the animals by nasopharyngeal washes. Approximately half of the animals inoculated with 10(7) CFU remained colonized 13 days after the initial bacterial inoculation. The model was further evaluated with genetically defined isogenic serogroup B mutant strains, and the colonization capabilities of the mutants were compared to that of the wild-type parent. A mutant that produces truncated lipooligosaccharide (KDO(2)-lipid A) and a mutant defective in capsule transport were dramatically impaired in colonization. A mutant defective in pilus transport (pilQ) showed moderately impaired colonization. The immunological aspect of the model was

also evaluated by challenging mice after immunization with homologous whole-cell meningococci. The immunized mice were protected from colonization of the homologous strain. In this model, long-term meningococcal colonization was maintained, allowing us to study the effects of specific genetic mutation on colonization. In addition, this model allows investigation of the role of active immune response against meningococci.

L35 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2003072324 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12581696
TITLE: Reproductive toxicity testing of vaccines.
AUTHOR: Verdier Francois; Barrow Paul C; Burge Joelle
CORPORATE SOURCE: Aventis Pasteur, Campus Merieux, 1541 avenue Marcel Merieux, 69280 Marcy l'Etoile, France.. francois.verdier@aventis.com
SOURCE: Toxicology, (2003 Apr 1) 185 (3) 213-9. Ref: 26
Journal code: 0361055. ISSN: 0300-483X.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030214
Last Updated on STN: 20030326
Entered Medline: 20030325

ED Entered STN: 20030214
Last Updated on STN: 20030326
Entered Medline: 20030325

AB Vaccines play a major role in the prevention of human birth defects by protecting the pregnant woman from teratogenic or otherwise harmful infections. Until now, it has not been common practice to perform preclinical developmental toxicity tests for new vaccines. Despite the excellent safety record of vaccines, increased attention is now being given to the feasibility of screening new vaccines for developmental hazards in animals before their use in humans. Contrary to previous assumptions, many vaccines are now given to potentially pregnant women. Any new components of the vaccine formulation (adjuvants, excipients, stabilisers, preservatives, etc.) could also be tested for influences on development, although based on past experience the risks are limited by the very low dosages used. The conferred immunity following vaccination lasts for several years. Therefore, the developing conceptus may theoretically be exposed to the induced antibodies and/or sensitised T-cells, even if the pregnant woman was last vaccinated during childhood (particularly if she encounters the antigen during pregnancy through exposure to infection). However, it should be kept in mind that viral or bacterial infections represent a higher risk for a pregnant woman than the potential adverse effects related to vaccination or the associated immune response. Non-clinical safety studies may be employed as an aid for hazard identification. In these studies interactions of the vaccine with the maternal immune system or with the developmental systems of the offspring are considered. Post-natal examinations are necessary to detect all

possible manifestations of developmental toxicity, such as effects on the immune system. Species selection for the preclinical studies is based on immunogenicity to the vaccine and the relative timing and rate of transfer of maternal antibodies to the offspring. A single study design is proposed for the pre- and post-natal developmental assessments of vaccines in rodents and rabbits.

L35 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2003011395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12517268
TITLE: Reverse vaccinology: a genome-based approach for vaccine development.
AUTHOR: Masignani Vega; Rappuoli Rino; Pizza Mariagrazia
CORPORATE SOURCE: IRIS, Chiron SPA, Via Fiorentina 1, 53100 Siena, Italy.
SOURCE: Expert opinion on biological therapy, (2002 Dec) 2 (8) 895-905. Ref: 89
Journal code: 101125414. ISSN: 1471-2598.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20030109
Last Updated on STN: 20031220
Entered Medline: 20031219
ED Entered STN: 20030109
Last Updated on STN: 20031220
Entered Medline: 20031219
AB During the last century several approaches have been followed for the development of vaccines. These include live-attenuated viruses and bacteria, killed microorganisms and the subunit vaccines [1]. With the introduction of recombinant DNA technologies, new approaches have been exploited for vaccine manufacturing. However, the major problem remains the rapid identification of highly immunogenic and protective antigens suitable for vaccine development, which still relies on standard biochemical and microbiological techniques. The advent of genomics has greatly contributed to providing a new impulse to the microbial field. The complete genomic sequence of a human pathogen represents a new unexploited field, to be used for the design of novel vaccines and antimicrobial drugs. In the case of meningococcus B, four decades of continuous efforts, using conventional technologies of purifying antigens from the microorganism, had not been sufficient to deliver an effective and universal vaccine. It was therefore decided to obtain the genomic sequence of serogroup B Neisseria meningitidis (MenB) and use this information to identify vaccine candidates. This approach was named "reverse vaccinology"[2].

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10/089583

key terms

L1 508 SEA FILE=CAPLUS ABB=ON PLU=ON (NEISSER? OR MENINGITID?) (S)((TYPE OR SEROTYPE OR GROUP)(2A)B)
L2 285 SEA FILE=CAPLUS ABB=ON PLU=ON MENINGOCOCC?(S)((TYPE OR SEROTYPE OR GROUP)(2A)B)
L16 82 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 OR L2) AND (PATHOGEN? (S)NEISSER? OR GONORRHOEAE OR GONOCOCC?)
L18 1 SEA FILE=CAPLUS ABB=ON PLU=ON L16 AND (GALE OR GAL E)

L1 508 SEA FILE=CAPLUS ABB=ON PLU=ON (NEISSER? OR MENINGITID?) (S)((TYPE OR SEROTYPE OR GROUP)(2A)B)
L2 285 SEA FILE=CAPLUS ABB=ON PLU=ON MENINGOCOCC?(S)((TYPE OR SEROTYPE OR GROUP)(2A)B)
L16 82 SEA FILE=CAPLUS ABB=ON PLU=ON (L1 OR L2) AND (PATHOGEN? (S)NEISSER? OR GONORRHOEAE OR GONOCOCC?)
L19 21 SEA FILE=CAPLUS ABB=ON PLU=ON L16 AND (LOS OR LPS OR LIPOPOLYSACCHARIDE OR LIPOOLIGOSACCHARIDE OR ENDOTOXIN OR LIPO(W)(POLYSACCHARIDE OR OLIGOSACCHARIDE OR (POLY OR OLIGO)(W)SACCHARIDE) OR (LIPOPOLY OR LIPOOLIGO)(W)SACCHARIDE)

L23 21 L18 OR L19

L23 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Jul 2004
ACCESSION NUMBER: 2004:527054 CAPLUS
TITLE: Human dendritic cell activation by Neisseria meningitidis: Phagocytosis depends on expression of **lipooligosaccharide** (**LOS**) by the bacteria and is required for optimal cytokine production
AUTHOR(S): Uronen-Hansson, Heli; Steeghs, Liana; Allen, Jennifer; Dixon, Garth L. J.; Osman, Mohamed; Van Der Ley, Peter; Wong, Simon Y. C.; Callard, Robin; Klein, Nigel
CORPORATE SOURCE: Immunobiology Unit, Institute of Child Health, UCL, London, UK
SOURCE: Cellular Microbiology (2004), 6(7), 625-637
CODEN: CEMIF5; ISSN: 1462-5814
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Group B Neisseria meningitidis** is a human **pathogen**, for which a universally effective vaccine is still not available. Immune responses to bacteria are initiated by dendritic cells (DC), which internalize and process bacterial antigens for presentation to T cells. We show here that optimal IL-12 and TNF-α production by human monocyte derived DC in response to killed serogroup B N. meningitidis depends on phys. contact and internalization of the bacteria by DC. The majority of DC producing cytokines had internalized N. meningitidis while inhibition of bacterial internalization markedly impaired IL-12 and TNF-α, but not IL-6 production Internalization of N. meningitidis was shown to depend on **lipooligosaccharide** (**LOS**)

Searcher : Shears 571-272-2528

expressed by the bacteria with poor internalization of **LOS** deficient bacteria compared to wild-type bacteria. Restoration of **LOS** biosynthesis in a **LOS** regulatory strain also restored both internalization and cytokine production and was enhanced in the presence of **LPS** binding protein (LBP). These results suggest that DC phagocytosis depends on expression of **LOS** within the bacteria and that optimal cytokine production, particularly IL-12, requires internalization of the bacteria. These findings have important implications for designing vaccines that will induce protective immune responses to **group B** N. **meningitidis**.

L23 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Feb 2004
ACCESSION NUMBER: 2004:142989 CAPLUS
DOCUMENT NUMBER: 140:180125
TITLE: Vaccine composition comprising transferrin binding protein and Hsf against Neisseria meningitidis, Neisseria **gonorrhoeae**, Moraxella catarrhalis and Haemophilus influenzae
INVENTOR(S): Berthet, Francois-xavier Jacques; Biemans, Ralph; Denoel, Philippe; Feron, Christiane; Goraj, Carine; Poolman, Jan; Weynants, Vincent
PATENT ASSIGNEE(S): Glaxosmithkline Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014419	A1	20040219	WO 2003-EP8567	20030731

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 2002-18035	A	20020802
GB 2002-18036	A	20020802
GB 2002-18037	A	20020802
GB 2002-18051	A	20020802
GB 2002-20197	A	20020830
GB 2002-20199	A	20020830
GB 2002-25524	A	20021101
GB 2002-25531	A	20021101
GB 2002-30164	A	20021224
GB 2002-30168	A	20021224
GB 2002-30170	A	20021224

GB 2003-5028 A 20030305

AB The present invention relates to immunogenic compns. and vaccines for the prevention or treatment of Gram neg. bacterial infection. Immunogenic compns. of the invention comprise transferrin binding protein and Hsf, and the combination of these two antigens have been shown to act synergistically to produce antibodies with high activity in a serum bactericidal assay. This combination of antigens is useful for use in vaccines against Neisseria meningitidis, Neisseria **gonorrhoeae**, Moraxella catarrhalis and Haemophilus influenzae.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Feb 2004
ACCESSION NUMBER: 2004:142988 CAPLUS
DOCUMENT NUMBER: 140:198065
TITLE: Vaccine compositions comprising Neisserial adhesin, autotransporter, toxin, iron acquisition protein and membrane-associated protein against Neisserial infection
INVENTOR(S): Berthet, Francois-xavier Jacques; Biemans, Ralph; Denoel, Philippe; Feron, Christiane; Goraj, Karine; Poolman, Jan; Weynants, Vincent
PATENT ASSIGNEE(S): Glaxosmithkline Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014418	A2	20040219	WO 2003-EP8571	20030731

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

GB 2002-18035	A	20020802
GB 2002-18036	A	20020802
GB 2002-18037	A	20020802
GB 2002-18051	A	20020802
GB 2002-20197	A	20020830
GB 2002-20199	A	20020830
GB 2002-25524	A	20021101
GB 2002-25531	A	20021101
GB 2002-30164	A	20021224

GB 2002-30168 A 20021224
GB 2002-30170 A 20021224
GB 2003-5028 A 20030305

AB The present invention relates to immunogenic compns. and vaccines for the treatment and prevention of Neisserial disease caused by e.g. Neisseria meningitidis or Neisseria **gonorrhoeae.** Immunogenic compns. of the invention contain combinations of antigens selected from at least two different classes of antigens including adhesins, autotransporter proteins, toxins, iron acquisitions proteins and membrane-associated protein (preferably integral outer membrane protein)s. Such combinations of antigens are able to target the immune response against different aspects of the neisserial life cycle, resulting in a more effective immune response.

L23 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 11 Aug 2003
ACCESSION NUMBER: 2003:613773 CAPLUS
DOCUMENT NUMBER: 139:225312
TITLE: Genetic characterization of pilin glycosylation and phase variation in Neisseria meningitidis
AUTHOR(S): Power, P. M.; Roddam, L. F.; Rutter, K.; Fitzpatrick, S. Z.; Srikhanta, Y. N.; Jennings, M. P.
CORPORATE SOURCE: Department of Microbiology and Parasitology, The University of Queensland, Brisbane, Australia
SOURCE: Molecular Microbiology (2003), 49(3), 833-847
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pili of Neisseria meningitidis are a key virulence factor, being the major adhesin of this capsulate organism and contributing to specificity for the human host. Pili are post-translationally modified by addition of either an O-linked trisaccharide, Gal (β1-4) Gal (α1-3) 2,4-diacetamido-2,4,6-trideoxyhexose or an O-linked disaccharide Gal (α1,3) GIcNAc. The role of these structures in meningococcal pathogenesis has not been resolved. In previous studies we identified two sep. genetic loci, pglA and pglBCD, involved in pilin glycosylation. Putative functions have been allocated to these genes; however, there are not enough genes to account for the complete biosynthesis of the described structures, suggesting addnl. genes remain to be identified. In addition, it is not known why some strains express the trisaccharide structure and some the disaccharide structure. In order to find addnl. genes involved in the biosynthesis of these structures, we used the recently published group A strain Z2491 and **group B** strain MC58 **Neisseria meningitidis** genomes and the unfinished **Neisseria meningitidis** group C strain FAM18 and **Neisseria gonorrhoeae** strain FA1090 genomes to identify novel genes involved in pilin glycosylation, based on homol. to known oligosaccharide biosynthetic genes. We identified a new gene involved in pilin glycosylation designated pglE and examined four addnl. genes pglB/B2, pglF, pglG and pglH. A strain survey revealed that pglE and pglF were present in each strain examined The pglG, pglH and pglB2 polymorphisms were not

found in strain C311#3 but were present in a large number of clin. isolates. Insertional mutations were constructed in pglE and pglF in N. meningitidis strain C311#3, a strain with well-defined **lipopolysaccharide** (**LPS**) and pilin-linked glycan structures. Increased gel migration of the pilin subunit mols. of pglE and pglF mutants was observed by Western anal., indicating truncation of the trisaccharide structure. Antisera specific for the C311#3 trisaccharide failed to react with pilin from these pglE and pglF mutants. GC-MS anal. of the sugar composition of the pgIE mutant showed a reduction in galactose compared with C311#3 wild type. Anal. of amino acid sequence homologies has suggested specific roles for pglE and pglF in the biosynthesis of the trisaccharide structure. Further, we present evidence that pglE, which contains heptanucleotide repeats, is responsible for the phase variation between trisaccharide and disaccharide structures in strain C311#3 and other strains. We also present evidence that pglG, pglH and pglB2 are potentially phase variable.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 14 Feb 2003
ACCESSION NUMBER: 2003:115601 CAPLUS
DOCUMENT NUMBER: 139:146243
TITLE: Nonencapsulated Neisseria meningitidis strain produces amylopectin from sucrose: altering the concept for differentiation between N. meningitidis and N. polysaccharea
AUTHOR(S): Zhu, Peixuan; Tsang, Raymond S. W.; Tsai, Chao-Ming
CORPORATE SOURCE: Division of Bacterial, Parasitic and Allergenic Products, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, Bethesda, MD, 20892, USA
SOURCE: Journal of Clinical Microbiology (2003), 41(1), 273-278
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neisseria meningitidis is the causative agent of meningococcal sepsis and meningitis. Neisseria polysaccharea is a nonpathogenic species. N. polysaccharea is able to use sucrose to produce amylopectin, a starch-like polysaccharide, which distinguishes it biochem. from the pathogenic species N. meningitides. The data presented here indicate that this may be an insufficient criterion to distinguish between these two species. The nonencapsulated Neisseria strain 93246 expressed a phenotype of amylopectin production similar to that of N. polysaccharea. However, strain 93246 reacted with N. meningitidis serotype 4 and serosubtype P1.14 monoclonal antibodies and showed the N. meningitides L1(8) **lipo-oligosaccharide** immunotype. Further analyses were performed on four genetic loci in strain 93246, and the results were compared with 7 N. meningitidis strains, 13 N. polysaccharea strains, and 2 N. **gonorrhoeae** strains. Three genetic loci, opcA, siaD,

and lgt-1 in strain 93246, were the same as in N. meningitides. Particularly, the siaD gene encoding polysialyltransferase responsible for biosynthesis of N. **meningitidis group B** capsule was detected in strain 93246. This siaD gene was inactivated by a frameshift mutation at the poly(C) tract, which makes strain 93246 identical to other nonencapsulated N. meningitidis strains. As expected, the ams gene encoding amylosucrase, responsible for production of amylopectin from sucrose, was detected in strain 93246 and all 13 N. polysaccharea strains but not in N. meningitidis and N. **gonorrhoeae** strains. These data suggest that strain 93246 is nonencapsulated N. meningitides but has the ability to produce extracellular amylopectin from sucrose. The gene for amylopectin production in strain 93246 was likely imported from N. polysaccharea by horizontal genetic exchange. Therefore, we conclude that genetic anal. is required to complement the traditional phenotypic classification for the nonencapsulated Neisseria strains.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 16 Aug 2001
ACCESSION NUMBER: 2001:594199 CAPLUS
DOCUMENT NUMBER: 135:287305
TITLE: Contributions of Neisseria meningitidis **LPS** and non-**LPS** to proinflammatory cytokine response
AUTHOR(S): Sprong, Tom; Stikkelbroeck, Nike; Van der Ley, Peter; Steeghs, Liana; Van Alphen, Loek; Klein, Nigel; Netea, Mihai G.; Van der Meer, Jos W. M.; Van Deuren, Marcel
CORPORATE SOURCE: Department of Internal Medicine, University Medical Center Nijmegen, Nijmegen, 6500 HB, Neth.
SOURCE: Journal of Leukocyte Biology (2001), 70(2), 283-288
CODEN: JLBIE7; ISSN: 0741-5400
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To determine the relative contribution of **lipopolysaccharide** (**LPS**) and non-**LPS** components of **Neisseria meningitidis** to the **pathogenesis** of **meningococcal** sepsis, this study quant. compared cytokine induction by isolated **LPS**, wild-**type** serogroup **B meningococci** (strain H44/76), and **LPS** -deficient mutant **meningococci** (strain H44/76[pLAK33]). Stimulation of human peripheral-blood mononuclear cells with wild-type and **LPS**-deficient meningococci showed that non-**LPS** components of meningococci are responsible for a substantial part of tumor necrosis factor (TNF)-α and interleukin (IL)-1β production and virtually all interferon (IFN)-γ production Based on tricine SDS-PAGE anal. of **LPS** in proteinase K-treated lysates of N. meningitidis H44/76, a quant.

comparison was made between the cytokine-inducing capacity of isolated and purified **LPS** and **LPS**-containing meningococci. At concns. of > 107 bacteria/mL, intact bacteria were more potent cytokine inductors than equivalent amts. of isolated **LPS**, and cytokine induction by non-**LPS** components was additive to that by **LPS**. Expts. with mice showed that non-**LPS** components of meningococci were able to induce cytokine production and mortality. The principal conclusion is that non-**LPS** parts of N. meningitidis may play a role in the pathogenesis of meningococcal sepsis by inducing substantial TNF-α, IL-1β, and IFN-γ production

REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 09 Feb 2001
ACCESSION NUMBER: 2001:101328 CAPLUS
DOCUMENT NUMBER: 134:146387
TITLE: Immuno-protective and non-toxic Gram-neg. bleb vaccine suitable for pediatric use
INVENTOR(S): Berthet, Francois-xavier Jacques; Dalemans, Wilfried L. J.; Denoel, Philippe; Dequesne, Guy; Feron, Christiane; Lobet, Yves; Poolman, Jan; Thiry, Georges; Thonnard, Joelle; Voet, Pierre
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009350	A2	20010208	WO 2000-EP7424	20000731
WO 2001009350	A3	20010830		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000012974	A	20020507	BR 2000-12974	20000731
TR 200200275	T2	20020521	TR 2002-20020027520000731	
EP 1208214	A2	20020529	EP 2000-956369	20000731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506049	T2	20030218	JP 2001-514142	20000731
AU 770360	B2	20040219	AU 2000-68336	20000731
EP 1307224	A2	20030507	EP 2001-965152	20010731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,				

PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
NO 2002000506 A 20020402 NO 2002-506 20020131
PRIORITY APPLN. INFO.: GB 1999-18319 A 19990803
WO 2000-EP7424 W 20000731
GB 2001-3170 A 20010208
WO 2001-EP8857 W 20010731

AB The present invention relates to an immuno-protective and non-toxic Gram-neg. bleb vaccine suitable for pediatric use. Examples of the Gram-neg. strains from which the blebs are made are N. meningitidis, M. catarrhalis and H. influenzae. The blebs of the invention are improved by one or more genetic changes to the chromosome of the bacterium, including up-regulation of protective antigens, down-regulation of immunodominant non-protective antigens, and detoxification of the Lipid A moiety of **LPS**.

L23 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 24 Feb 2000
ACCESSION NUMBER: 2000:125480 CAPLUS
DOCUMENT NUMBER: 132:263740
TITLE: The contrasting mechanisms of serum resistance of **Neisseria gonorrhoeae** and **group B Neisseria meningitidis**
AUTHOR(S): Ram, S.; Mackinnon, F. G.; Gulati, S.; McQuillen, D. P.; Vogel, U.; Frosch, M.; Elkins, C.; Guttormsen, H.-K.; Wetzler, L. M.; Oppermann, M.; Pangburn, M. K.; Rice, P. A.
CORPORATE SOURCE: The Maxwell Finland Laboratory for Infectious Diseases, Boston Medical Center, Boston, MA, 02118, USA
SOURCE: Molecular Immunology (1999), 36(13-14), 915-928
CODEN: MOIMD5; ISSN: 0161-5890
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 159 refs. Neisseria **gonorrhoeae** and Neisseria meningitidis have evolved intricate mechanisms to evade complement-mediated killing. Sialylation of **gonococcal lipooligosaccharide** (**LOS**) results in conversion of previously serum sensitive strains to unstable serum resistance, which is mediated by factor H binding. Porin (Por) is also instrumental in mediating stable serum resistance in **gonococci**. The 5th loop of certain **gonococcal** Por1As binds factor H, which efficiently inactivates C3b to iC3b. Factor H glycan residues may be essential for factor H binding to certain Por1A strains. Por1A strains can also regulate the classical pathway by binding to C4b-binding protein (C4bp) probably via the 1st loop of the Por mol. Certain serum resistant Por1B strains can also regulate complement by binding C4bp through a loop other than loop 1. Purified C4b can inhibit binding of C4bp to Por1B, but not Por1A, suggesting different binding sites on C4bp for the two Por types. Unlike serum resistant **gonococci**, resistant meningococci have abundant C3b on their surface, which is only partially processed to iC3b. The main mechanism of complement evasion by **group B meningococci** is inhibition of membrane attack complex (MAC) insertion by their

polysaccharide capsule. **LOS** structure may act in concert with capsule to prevent MAC insertion. Meningococcal strains with Class 3 Por preferentially bind factor H, suggesting Class 3 Por acts as a receptor for factor H.

REFERENCE COUNT: 161 THERE ARE 161 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 02 Aug 1997
ACCESSION NUMBER: 1997:482780 CAPLUS
DOCUMENT NUMBER: 127:204145
TITLE: Neisserial porins may provide critical second signals to polysaccharide-activated murine B cells for induction of immunoglobulin secretion
AUTHOR(S): Snapper, Clifford M.; Rosas, Fabio R.; Kehry, Marilyn R.; Mond, James J.; Wetzler, Lee M.
CORPORATE SOURCE: Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, MD, 20814, USA
SOURCE: Infection and Immunity (1997), 65(8), 3203-3208
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Resting B cells stimulated with dextran-conjugated anti-IgD (anti-IgD) antibodies (anti-Ig-dex), a model for B-cell activation in response to polysaccharide antigens, proliferate but secrete little if any Ig, unless addnl. stimuli are present. In order to elucidate the parameters which costimulate T-cell-independent antipolysaccharide antibody responses during bacterial infections, we tested the capacities of highly purified porin proteins from Neisseria meningitidis and Neisseria **gonorrhoeae** to augment in vitro proliferation and induce Ig secretion by anti-Ig-dex-activated B cells. Resting B cells, from **lipopolysaccharide** (**LPS**)-nonresponsive C3H/HeJ mice, proliferated and secreted IgM in response to each of three distinct porins acting alone. Further, porins, even at concns. that were minimally inductive when acting alone, were strongly synergistic with anti-Ig-dex for proliferation and Ig secretion. Similar synergistic effects of porins with CD40-ligand were also observed These effects of porins were shown to occur directly at the level of the B cell. The predominant Ig isotype elicited in response to porins plus anti-Ig-dex or CD40-ligand was IgM (>97%), with the remainder comprising IgG. Surprisingly, picogram-per-milliliter amts. of neisserial **LPS** were also found to be highly synergistic with anti-Ig-dex for induction of IgM secretion by **LPS**-responsive C3H/HeN, but not C3H/HeJ, B cells. Thus, these data suggest that porins, as well as **LPS**, may provide critical second signals for T-cell-independent induction of polysaccharide-specific Ig in response to **neisserial** and other gram-neg. porin-expressing bacterial **pathogens**, without a requirement for the participation of non-**B** cell **types**. These data may also help to explain the potent immunopotentiating effects of porins for polysaccharide-specific, as well as protein-specific, humoral responses in vivo.

L23 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 May 1997
ACCESSION NUMBER: 1997:290539 CAPLUS
DOCUMENT NUMBER: 126:263152
TITLE: Improved methods for the production of non-covalently complexed and multivalent proteosome sub-unit vaccines
INVENTOR(S): Lowell, George H.; Zollinger, Wendell D.; Wood, James F.
PATENT ASSIGNEE(S): United States Army Medical Research Material Command, USA; Lowell, George H.; Zollinger, Wendell D.; Wood, James F.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9710844	A1	19970327	WO 1996-US15002	19960918
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM				
CA 2232410	AA	19970327	CA 1996-2232410	19960918
CA 2232410	C	20030617		
AU 9671131	A1	19970409	AU 1996-71131	19960918
EP 854729	A1	19980729	EP 1996-932269	19960918
EP 854729	B1	20040310		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1211192	A	19990317	CN 1996-197616	19960918
JP 2000507913	T2	20000627	JP 1997-512875	19960918
BR 9610484	A	20010911	BR 1996-10484	19960918
IL 123720	A1	20020210	IL 1996-123720	19960918
AT 261313	E	20040315	AT 1996-932269	19960918
NO 9801189	A	19980514	NO 1998-1189	19980317
US 6476201	B1	20021105	US 1998-43529	19980727
US 2002164357	A1	20021107		
AU 751063	B2	20020808	AU 2000-61234	20000921
AU 2000061234	A5	20001130		
JP 2004099619	A2	20040402	JP 2003-365270	20031024

PRIORITY APPLN. INFO.: US 1995-3859P P 19950918
JP 1997-512875 A3 19960918
WO 1996-US15002 W 19960918

AB A method for preparing multivalent proteosome-amphiphilic determinant vaccines suitable for parenteral or mucosal administration using diafiltration or ultrafiltration technol. The amphiphilic determinants include **lipopolysaccharides** from gram neg. bacteria, e.g. Shigella Flexneri, Plesiomonas shigelloides and

Shigella sonnei. Proteosomes are obtained from **group B type** 2b **meningococci**. The active proteosome-amphiphilic determinant complexes (non-covalently complexes) of the vaccine are formed using diafiltration or ultrafiltration to remove the detergent. The use of diafiltration or ultrafiltration decreases processing time and the opportunity for contamination and further permits the use of ambient temperature and efficient scale-up. In addition, the process permits the reliable and continuous monitoring of the dialyzate which enhances the efficiency of the entire process. The time of dialysis for production of a lot of vaccine is reduced from >7-10 days to less than 72 h and usually less than 48 or 24 h. The use of the process optimizes the presence of each antigenic component in the preparation of multivalent vaccines.

L23 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 06 Nov 1996
ACCESSION NUMBER: 1996:655135 CAPLUS
DOCUMENT NUMBER: 125:296790
TITLE: Sialic acids of both the capsule and the sialylated **lipooligosaccharide** of Neisseria meningitis serogroup B are prerequisites for virulence of meningococci in the infant rat
AUTHOR(S): Vogel, Ulrich; Hammerschmidt, Sven; Frosch, Matthias
CORPORATE SOURCE: Institut fur Medizinische Mikrobiologie, Medizinische Hochschule Hannover, Hannover, D-30623, Germany
SOURCE: Medical Microbiology and Immunology (1996), 185(2), 81-87
CODEN: MMIYAO; ISSN: 0300-8584
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors investigated the contribution of the polysialic acid capsule and of terminal **lipooligosaccharide** (**LOS**) sialylation to the **pathogenicity** of **Neisseria** meningitidis in vivo using a set of defined isogenic mutants of the N. meningitidis strain B 1940 deficient in either capsule synthesis or **LOS** sialylation. Furthermore a spontaneous capsule-deficient variant was investigated, which was capable of switching on the capsule synthesis at a frequency of 3+10-3 in vitro. Infection of infant rats with the wild-type strain revealed a high potential to cause bacteremia. This potential was attenuated in the capsule-phase variable mutant (**LOS** sialylation+). However, using a mutant irreversibly deficient in capsule synthesis, but expressing a sialylated **LOS**, bacteremia could only be achieved using 106 times higher nos. of bacteria when compared to the wild-type. The unencapsulated bacteria were located extracellularly upon examination of blood smears, suggesting that defense mechanisms, i.e. phagocytosis, directed against unencapsulated meningococci were exhausted using very high infecting doses. Interestingly, when infant rats were infected with encapsulated meningococci which were unable to sialylate the **LOS**, bacteremia could never be achieved, even with an infective dose as high as 108 colony forming units (CFU). Despite the presence of

capsular polysaccharide this mutant was phagocytosed by peritoneal phagocytes, as was the unencapsulated, **LOS**-sialylated mutant, suggesting that the inability to cause bacteremia was due to a higher susceptibility to the action of the complement system, which is virtually unsaturable. The authors conclude that in the infant rat model of meningococcal infection both forms of sialic acid on the bacterial cell surface are indispensable for systemic survival.

L23 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Nov 1994
ACCESSION NUMBER: 1995:20020 CAPLUS
DOCUMENT NUMBER: 122:75073
TITLE: Tn916-generated, **lipooligosaccharide** mutants of Neisseria meningitidis and Neisseria **gonorrhoeae**
AUTHOR(S): Stephens, D. S.; McAllister, C. F.; Zhou, D.; Lee, F. K.; Apicella, M. A.
CORPORATE SOURCE: Sch. Medicine, Emory Univ., Atlanta, GA, USA
SOURCE: Infection and Immunity (1994), 62(7), 2947-52
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A library of Tn916-generated, tetracycline-resistant (Tcr) mutants of the **group B Neisseria meningitidis** strain NMB was screened by using monoclonal antibodies (MAbs) that recognize structural differences in **neisserial lipooligosaccharide** (**LOS**). The **LOS** of parental strain NMB had a relative mol. mass of 4.5 kDa, reacted with MAbs 3F11 and 6B4 but not with MAb 4C4 or 6E4, and contained a lacto-N-neotetrose unit. Two phenotypically stable mutants, SS3 and R6, altered in **LOS**, were identified by colony immunoblots, electrophoresis, and Western immunoblots. The **LOS** of mutant SS3 was 3.4 kDa and reacted with MAbs 4C4 and 6E4 but not MAb 3F11 or 6B4. The **LOS** of mutant R6 was 3.1 to 3.2 kDa and reacted with MAb 6E4 but not MAb 3F11, 6B4, or 4C4. Thus, the LOSs of the R6 and SS3 mutants were predicted to contain different truncations of the core oligosaccharide. The **LOS** phenotype of each mutant was linked to Tcr, as determined by transformation of the parent strain with DNA from the mutant. Southern hybridizations and single-specific-primer PCR revealed in each mutant a single truncated Tn916 insertion which had lost genes required for mobilization. Tn916 mutagenesis was used to identify two distinct genetic sites in the meningococcal chromosome involved in biosynthesis of the oligosaccharide chain of **LOS** and to create genetically defined **LOS** mutants of N. meningitidis and Neisseria **gonorrhoeae**.

L23 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 28 Jun 1991
ACCESSION NUMBER: 1991:244001 CAPLUS
DOCUMENT NUMBER: 114:244001
TITLE: Endogenous sialylation of the **lipooligosaccharides** of Neisseria meningitidis
AUTHOR(S): Mandrell, R. E.; Kim, J. J.; John, C. M.;

Gibson, B. W.; Sugai, J. V.; Apicella, M. A.; Griffiss, J. M.; Yamasaki, R.
CORPORATE SOURCE: Cent. Immunochem., Veterans Adm. Med. Cent., San Francisco, CA, 94121, USA
SOURCE: Journal of Bacteriology (1991), 173(9), 2823-32
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Monoclonal antibodies (MAb) 3F11 and 06B4 recognize epitopes that are conserved on **gonococcal lipooligosaccharides** (**LOS**), present on some meningococcal **LOS**, and conserved on human erythrocytes. **LOS** of some **group B** and C prototype **meningococcal** **LOS** strains (**LOS** serotypes L1-L8) treated with neuraminidase showed increased expression of the 3F11 and 06B4 MAb-defined epitopes. Neuraminidase-treated **LOS** separated by SDS-PAGE and silver-stained showed a shift in migration from a component with a mass of .apprx.4.8 kDa to a component with a mass of 4.5-4.6 kDa. The same strains grown in medium with excess CMP-N-acetylneuraminic acid had **LOS** that shifted in migration to a slightly higher component (mass .apprx.4.8 kDa). Chemical anal. of the neuraminidase-digested products from 1 **LOS** indicated it contained .apprx.1.5% sialic acid. Covalent linkage between sialic acid and the **LOS** was confirmed by anal. of de-O-acylated and dephosphorylated **LOS** by liquid secondary ion mass spectrometry. These studies show that some meningococci contain sialic acid in their **LOS**, that the sialic acid is cleaved and lost in conventional HOAc hydrolysis, and that the sialic acid alters the expression of MAb-defined epitopes.

L23 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 05 Mar 1988
ACCESSION NUMBER: 1988:73342 CAPLUS
DOCUMENT NUMBER: 108:73342
TITLE: Synergistic effect of detergents and aluminum phosphate on the humoral immune response to bacterial and viral membrane proteins
AUTHOR(S): Teerlink, Tom; Beuvery, E. Coen; Evenberg, Dolf; Van Wezel, Toon L.
CORPORATE SOURCE: Dep. Bact. Vaccines, Natl. Inst. Public Health Environ. Hyg. (RIVM), Bilthoven, 3720 BA, Neth.
SOURCE: Vaccine (1987), 5(4), 307-14
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The influence of detergents on the immunogenic activity of the major outer membrane protein of Neisseria **gonorrhoeae** was investigated. Most detergents tested enhanced the immune response. This effect was synergistic with the adjuvant activity of AlPO4. The combination of detergent and AlPO4 showed a stronger adjuvant activity than Freund's complete adjuvant. The adjuvant effect was only observed with protein prepns. with very low **lipopolysaccharide** content. The immunostimulating effect of detergents was also observed with **meningococcal** group C polysaccharide conjugated to a Haemophilus influenzae **type**

b outer membrane protein and with the fusion protein of measles virus. The influence of some detergent parameters (critical micelle concentration, hydrophile-lipophile balance, and charge) was investigated.

L23 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 03 May 1986
ACCESSION NUMBER: 1986:146768 CAPLUS
DOCUMENT NUMBER: 104:146768
TITLE: Definition of a virulence-related antigen of Neisseria **gonorrhoeae** with monoclonal antibodies and lectins
AUTHOR(S): Demarco de Hormaeche, Raquel; Bundell, Christine; Chong, Hueng; Taylor, David W.; Wildy, Peter
CORPORATE SOURCE: Dep. Pathol., Univ. Cambridge, Cambridge, UK
SOURCE: Journal of Infectious Diseases (1986), 153(3), 535-46
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Variants of one strain of N. **gonorrhoeae**, grown in vivo or in vitro, that had been previously shown to differ in infectivity, serum resistance, and capsule production were compared with use of monoclonal antibodies and lectins. Monoclonal antibodies to virulent **gonococci** recognized an antigenic site of the **lipopolysaccharide** (**LPS**) produced in large amts. by **gonococci** grown in vivo but present only in a small proportion of in vitro-grown **gonococci**. This antigen (C-**LPS**) was found in all 85 different **gonococcal** isolates studied but not among nonpathogenic neisseriae. It was shared by **group B** and C **meningococci** but not by groups A and D. ELISA and Western blot anal. showed that N-acetylglucosamine and N-acetylgalactosamine form part of the epitope. The C-**LPS** antigen was shown by immunofluorescence to be present on the surface of the **gonococci** and also free as slime. This antigen appears to confer resistance to killing by normal sera.

L23 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 09 Mar 1985
ACCESSION NUMBER: 1985:76851 CAPLUS
DOCUMENT NUMBER: 102:76851
TITLE: Affinity chromatography for purification of antibodies to Neisseria **gonorrhoeae** and Neisseria meningitidis **lipopolysaccharides**
AUTHOR(S): Roedahl, Eyvind; Maeland, Johan A.
CORPORATE SOURCE: Fac. Med., Univ. Trondheim, Trondheim, 7000, Norway
SOURCE: Acta Pathologica, Microbiologica et Immunologica Scandinavica, Section C: Immunology (1984), 92C(5), 247-54
CODEN: APMIDO; ISSN: 0108-0202
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Lipopolysaccharides** (LPSs) were prepared by phenol-water extraction of the **gonococcal** strain 8551 and the **group B meningococcal** strain 44/76, digested with Pronase, and purified by ultracentrifugation and Sepharose CL-6B fractionation in the presence of 1.5% SDS. On SDS-polyacrylamide gel electrophoresis (PAGE) with 10% acrylamide the purified 125I-labeled LPSs migrated as single, low-mol.-weight components. The LPSs were coupled to CNBr-activated Sepharose 4B for affinity purification of antibodies to the common antigenic factor 1 and the sero-type factor 5 of **LPS** 8551, and antibodies to **LPS** 44/76. The antibodies eluted showed ELISA activity against wells coated with **LPS** or whole cells of the bacteria, the antibody activity being inhibited by **LPS**. SDS-PAGE of whole cells of the strain 8551 and immunoblotting with the anti-factor 1 or -factor 5 antibodies resulted in single, broad bands corresponding to the low-mol.-weight **LPS** subunits.

L23 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1984:83826 CAPLUS
DOCUMENT NUMBER: 100:83826
TITLE: Enzyme-linked immunosorbent assay with a monoclonal antibody for detecting group A meningococcal antigens in cerebrospinal fluid
AUTHOR(S): Sugasawara, Renee J.; Prato, Catherine M.; Sippel, John E.
CORPORATE SOURCE: Berkeley, Sch. Public Health, Univ. California, Oakland, CA, 94625, USA
SOURCE: Journal of Clinical Microbiology (1984), 19(2), 230-4
CODEN: JCMIDW; ISSN: 0095-1137
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hybridomas were produced from spleen cells of BALB/c mice immunized with a membrane preparation from Neisseria meningitidis group A strain 4402 and S194/5.XXOBU.14 myeloma cells. The hybridomas were screened for secretion of antibodies suitable for an ELISA diagnostic for group A meningococcal meningitis. One hybridoma antibody, 3G7, was directed against the pilus protein. This antibody bound to all 6 **lipopolysaccharide** and protein group A **meningococcal** of Escherichia coli, Haemophilus influenzae **type b**, or to ≥2 strains of Streptococcus pneumoniae, N. **gonorrhoeae**, and Salmonella typhi. The ELISA used an antibody, antigen, antibody-conjugate sandwich. Rabbit anti-meningococcal serum was the coating antibody for the antibody sandwich. Cerebrospinal fluids contained the bacterial antigens, and 3G7-alkaline phosphatase conjugate was the detecting antibody. The monoclonal antibody conjugate ELISA system detected group A meningococcal antigens in 21 of 25 cerebrospinal fluid specimens that were pos. in an immune rabbit serum conjugate ELISA. Counterimmunoelectrophoresis detected meningococcal antigens in 16 of the same 25 cerebrospinal fluid samples.

L23 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1984:33094 CAPLUS

DOCUMENT NUMBER: 100:33094
TITLE: Monoclonal antibodies against Neisseria meningitidis **lipopolysaccharide**
AUTHOR(S): Sugasawara, Renee J.; Prato, Catherine; Sippel, John E.
CORPORATE SOURCE: Nav. Biosci. Lab., Univ. California, Oakland, CA, 94625, USA
SOURCE: Infection and Immunity (1983), 42(3), 863-8
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cell line producing monoclonal antibodies directed against a **lipopolysaccharide** component of N. meningitidis group A was established. These antibodies reacted with only 1 of 3 **lipopolysaccharide** serotyping strains of group A meningococci by coagglutination, ELISA, and Western blotting techniques. A Western blot anal. showed that a NaOH digest of **lipopolysaccharide** was detectable by the serotype-specific antibody. The monoclonal antibodies cross-reacted with a **group B meningococcal** strain in an ELISA. The immunoblotting anal. also showed that these antibodies reacted with the **lipopolysaccharides** of a **group B meningococcus** as well as Haemophilus influenzae **type B,** but not with the **lipopolysaccharides** of several strains of Salmonella typhi, Escherichia coli, Streptococcus pneumoniae, and N. **gonorrhoeae.**

L23 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1979:555884 CAPLUS
DOCUMENT NUMBER: 91:155884
TITLE: **Lipopolysaccharide**-derived serotype polysaccharides from **Neisseria meningitidis group B**
AUTHOR(S): Apicella, Michael A.
CORPORATE SOURCE: Sch. Med., State Univ. New York, Buffalo, NY, USA
SOURCE: Journal of Infectious Diseases (1979), 140(1), 62-72
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three immunolog. distinct types of polysaccharides were isolated by DEAE-Sepharose column chromatog. from the **lipopolysaccharide** exts. of **group B** N. **meningitidis.** All types contained a set of common determinants, as well as distinct ones; all of these determinants were detectable by either immunodiffusion or enzyme-linked immunosorbent assay (ELISA). The polysaccharides eluted from a Sepharose 4B column in the range of 2-3 + 105 daltons and had isoelec. points from 4.2 to 4.3. Their antigenicity was destroyed by oxidation but was unaffected by neuraminidase, lysozyme, or trypsin. One type of polysaccharide cross-reacted with the Gc2 polysaccharide of N. **gonorrhoeae** in immunodiffusion systems. These polysaccharides contained hexoses, hexosamines, 2-keto-3-deoxyoctonate, ethanolamine, and

<0.05% proteins. In contrast to the **lipopolysaccharide** from which they are derived, these polysaccharides contained no lipid A and <0.5% fatty acids. All 3 types were precipitated by wheat germ agglutinin but not by concanavalin A or fucose-binding protein. Specific inhibition of this precipitation was achieved with N-acetyl glucosamine. These antigens may be the basis for a **lipopolysaccharide**-derived typing system for **group B** N. **meningitidis**.

L23 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1978:487493 CAPLUS
DOCUMENT NUMBER: 89:87493
TITLE: The critical role of iron in host-bacterial interactions
AUTHOR(S): Payne, Shelley M.; Finkelstein, Richard A.
CORPORATE SOURCE: Dep. Microbiol., Univ. Texas Southwest. Med. Sch., Dallas, TX, USA
SOURCE: Journal of Clinical Investigation (1978), 61(6), 1428-40
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of potential pathogens to acquire Fe in a host is an important determinant of both their virulence and the nature of the infection produced. Virulent gram-neg. bacteria are capable of acquiring sufficient Fe from the host since their virulence (for chick embryos) is unaffected by exogenous Fe. Avirulent mutants which are apparently limited in their ability to acquire Fe were isolated from the virulent strains. The lethality of these mutants was enhanced by exogenous Fe. Reduction of the relatively high serum Fe saturation of chick embryos (to levels more closely approximating those in man) by pretreatment with Fe-binding proteins or **endotoxin** inhibited the lethality of some virulent bacteria. Those bacteria whose virulence was reduced included Shigella, Vibrio cholerae, and strains of **Neisseria gonorrhoeae**, all of which are nondisseminating **pathogens** in the normal human host. **Pathogens** which produce septicemic and disseminating infections such as **Neisseria meningitidis**, Haemophilus influenzae **type B**, Escherichia coli possessing K-1 antigen, Pseudomonas aeruginosa, and Salmonella typhimurium and disseminating strains of N. **gonorrhoeae** were, in general, unaffected by reduced serum Fe saturation These disseminating bacteria appeared to produce greater quantities of compds. (siderophores) which stimulated microbial growth in low-Fe media than did the nondisseminating pathogens. Thus, the gram-neg. bacteria tested can be divided into 4 major classes according to their responses to modifications in Fe levels in the chick embryo model, and these results correlate with the nature of the infections which they typically produce in man.

L23 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1978:440649 CAPLUS
DOCUMENT NUMBER: 89:40649
TITLE: Degradation of the polysaccharide component of

gonococcal lipopolysaccharide
by **gonococcal** and meningococcal sonic extracts

AUTHOR(S): Apicella, Michael A.; Breen, John F.; Gagliardi, Nick C.
CORPORATE SOURCE: Dep. Med., State Univ. New York, Buffalo, NY, USA

SOURCE: Infection and Immunity (1978), 20(1), 228-34
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An extract made from the supernatant of Neisseria **gonorrhoeae** Gc2 strain 1291 degraded the Gc2 polysaccharide antigen. Chemical anal. of this polysaccharide indicated it contains glucose, galactose, glucosamine, galactosamine, glucosamine-6-phosphate, heptose, 2-keto-3-deoxyoctonate, and ethanolamine and is the polysaccharide of **gonococcal lipopolysaccharide**. Degradation of the polysaccharide by sonic exts. resulted either in complete loss of antigenicity and immunogenicity or in partial degradation to subunits that could inhibit the Gc2-specific hemagglutination inhibition. The factors responsible for degradation were destroyed by heating at 100° for 5 min or by pronase digestion, but were unaffected by RNase, DNase, Mg2+, Ca2+, or EDTA. The process was pH dependent, with optimal activity occurring at pH 7. Sonic extract supernatants from **group B** and C **meningococcal** strains contained degrading properties, whereas similar exts. produced from Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, and Streptococcus pneumoniae type II failed to degrade the Gc2 polysaccharide.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 15:46:02 ON 14 JUL 2004)

L20 97 S L19
L21 44 S L20 AND ANTIBOD?
L22 4 S L18

L24 46 S L21 OR L22

DUPLICATE IS NOT AVAILABLE IN 'FEDRIP'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L24
L25 27 DUP REM L24 (19 DUPLICATES REMOVED)

L25 ANSWER 1 OF 27 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003037563 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12517860
TITLE: Nonencapsulated Neisseria meningitidis strain produces amylopectin from sucrose: altering the concept for differentiation between N. meningitidis and N. polysaccharea.
AUTHOR: Zhu Peixuan; Tsang Raymond S W; Tsai Chao-Ming
CORPORATE SOURCE: Division of Bacterial, Parasitic and Allergenic Products, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, Bethesda, Maryland 20892, USA.. Zhu@cber.fda.gov

Searcher : Shears 571-272-2528

CONTRACT NUMBER: 369VFFD018551 (FDA)
SOURCE: Journal of clinical microbiology, (2003 Jan) 41 (1) 273-8.
Journal code: 7505564. ISSN: 0095-1137.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030128
Last Updated on STN: 20030508
Entered Medline: 20030507

AB Neisseria meningitidis is the causative agent of meningococcal sepsis and meningitis. Neisseria polysaccharea is a nonpathogenic species. N. polysaccharea is able to use sucrose to produce amylopectin, a starch-like polysaccharide, which distinguishes it biochemically from the pathogenic species N. meningitidis. The data presented here indicate that this may be an insufficient criterion to distinguish between these two species. The nonencapsulated Neisseria strain 93246 expressed a phenotype of amylopectin production similar to that of N. polysaccharea. However, strain 93246 reacted with N. meningitidis serotype 4 and serosubtype P1.14 monoclonal **antibodies** and showed the N. meningitidis L1(8) **lipo-oligosaccharide** immunotype. Further analyses were performed on four genetic loci in strain 93246, and the results were compared with 7 N. meningitidis strains, 13 N. polysaccharea strains, and 2 N. **gonorrhoeae** strains. Three genetic loci, opcA, siaD, and lgt-1 in strain 93246, were the same as in N. meningitidis. Particularly, the siaD gene encoding polysialyltransferase responsible for biosynthesis of N. **meningitidis group B** capsule was detected in strain 93246. This siaD gene was inactivated by a frameshift mutation at the poly(C) tract, which makes strain 93246 identical to other nonencapsulated N. meningitidis strains. As expected, the ams gene encoding amylosucrase, responsible for production of amylopectin from sucrose, was detected in strain 93246 and all 13 N. polysaccharea strains but not in N. meningitidis and N. **gonorrhoeae** strains. These data suggest that strain 93246 is nonencapsulated N. meningitidis but has the ability to produce extracellular amylopectin from sucrose. The gene for amylopectin production in strain 93246 was likely imported from N. polysaccharea by horizontal genetic exchange. Therefore, we conclude that genetic analysis is required to complement the traditional phenotypic classification for the nonencapsulated Neisseria strains.

L25 ANSWER 2 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:572006 BIOSIS
DOCUMENT NUMBER: PREV200200572006
TITLE: Structural analysis of the **lipopolysaccharide** from Neisseria meningitidis strain BZ157 **galE** : Localisation of two phosphoethanolamine residues in the inner core oligosaccharide.
AUTHOR(S): Cox, Andrew D. [Reprint author]; Li, Jianjun; Brisson, Jean-Robert; Moxon, E. Richard; Richards,

James C.
CORPORATE SOURCE: Institute for Biological Sciences, National Research Council, 100 Sussex Drive, Rm. 3089, Ottawa, ON, K1A 0R6, Canada
andrew.cox@nrc.ca
SOURCE: Carbohydrate Research, (9 September, 2002) Vol. 337, No. 16, pp. 1435-1444. print.
CODEN: CRBRAT. ISSN: 0008-6215.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002
AB The structure of the phase-variable **lipopolysaccharide** (**LPS**) from the **group B Neisseria meningitidis** strain BZ157 **galE** was elucidated. The structural basis for the **LPS**'s variation in reactivity with a monoclonal **antibody** (MAb) B5 that has specificity for the presence of phosphoethanolamine (PEtn) at the 3-position of the distal heptose residue (HepII) was established. The structure of the O-deacylated **LPS** was deduced by a combination of monosaccharide analyses, nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry. These analyses revealed the presence of a novel inner core oligosaccharide (OS) structure in the MAb B5 reactive (B5 +) **LPS** that contained two PEtn residues simultaneously substituting the 3- and 6-positions of the HepII residue. The determination of this structure has identified a further degree of variability within the inner core OS of meningococcal **LPS** that could contribute to the interaction of meningococcal strains with their host.

L25 ANSWER 3 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:585455 BIOSIS
DOCUMENT NUMBER: PREV200200585455
TITLE: Constrained cyclic peptides elicit cross-reactive **antibody** responses to **group B meningococcal lipooligosaccharide**.
AUTHOR(S): Tiwana, H. [Reprint author]; Feavers, I. M.; Charalambous, B. M. [Reprint author]
CORPORATE SOURCE: Medical School, Royal Free and University College, London, UK
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2002) Vol. 102, pp. 173. print.
Meeting Info.: 102nd General Meeting of the American Society for Microbiology. Salt Lake City, UT, USA. May 19-23, 2002. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002
AB **Neisseria** meningitidis is a human opportunistic **pathogen** for which no fully effective vaccine is available.

Vaccines based on the capsular polysaccharides from **meningococci** of serogroups A, C, Y and W135 have been developed, but the **group B** polysaccharide is poorly immunogenic since it mimics human cell surface antigens. As one alternative the meningococcal outer membrane **lipooligosaccharide** (**LOS**) contains epitopes that are immunogenic in man and has therefore been proposed as a potential vaccine component. Using a monoclonal **antibody**, 9-2-L379, specific for the **LOS** L3,7,9 immunotype that is most frequently associated with disease, linear and constrained cyclic peptides were identified from panning phage display libraries. Detailed characterisation of these peptides revealed that only constrained cyclic peptides were specific, bound with high apparent affinity and were able to inhibit binding of mAb 9-2-L379 to its nominal antigen, **LOS**. Data will be presented on immunisation experiments in C3H/HeN mice with one of the cyclic peptides biotinylated and complexed to Neutravidin as carrier protein. Standard conjugation procedures were not used as these eliminated the antigenicity of our cyclic peptide. Total and subclass IgG **antibodies** were analysed by ELISA with either the cyclic peptide or meningococcal **LOS** as target antigens. The predominant cross-reactive **antibody** responses to **LOS** were IgG1 and IgG2b. A positive correlation was observed between the IgG anti-peptide responses and the cross-reactive IgG anti-**LOS** responses. We have identified a structurally constrained cyclic peptide from phage panning and detailed biochemical and structural characterisation, which elicits **antibodies** that cross-react with the meningococcal carbohydrate antigen, **LOS**. Further studies to look at other cyclic peptides is underway, as well as investigating the function of the **antibodies** elicited against **LOS**.

L25 ANSWER 4 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-281657 [29] WPIDS
DOC. NO. CPI: C2001-085607
TITLE: Vaccine used for treating and preventing Neisseria infections, particularly N. meningitidis, comprises component of inner core **lipopolysaccharide** widely conserved among strains.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): COX, A D; GIDNEY, M A J; JENNINGS, M P; MOXON, E R; PLESTED, J S; RICHARDS, J C
PATENT ASSIGNEE(S): (ISIS-N) ISIS INNOVATION LTD
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001022994	A2	20010405	(200129)*	EN	81

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN

YU ZA ZW
AU 2000078023 A 20010430 (200142)
EP 1220686 A2 20020710 (200253) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK
NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001022994	A2	WO 2000-GB3758	20001002
AU 2000078023	A	AU 2000-78023	20001002
EP 1220686	A2	EP 2000-968062	20001002
		WO 2000-GB3758	20001002

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000078023	A	Based on	WO 2001022994
EP 1220686	A2	Based on	WO 2001022994

PRIORITY APPLN. INFO: US 2000-196305P 20000412; US 1999-156940P 19990930

AN 2001-281657 [29] WPIDS

AB WO 200122994 A UPAB: 20010528

NOVELTY - Vaccine (A) comprises an immunogenic component (I) based on the inner core of a Neisseria **lipopolysaccharide** (**LPS**) and is able to elicit functional **antibodies** (Ab) against most strains of a particular Neisseria species.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) vaccine (A1) comprising a few (I) and having properties similar to (A);

(b) **antibody** (Ab1) reactive with (I);

(c) hybridomas that produce the Ab1 designated B5 and A4;

(d) identifying immunogenic epitopes of strains of a particular Neisseria species by generating **antibodies** to the inner core of the bacterium and testing these against a wild-type N. meningitidis strain to identify reactive **antibodies** (i.e. those for which the epitope is accessible); and

(e) use of one or more biosynthetic pathway genes in preparation of a Neisseria strain for assessment, treatment or prevention of infections.

ACTIVITY - Antibacterial; antiinflammatory.

Infant rats were treated simultaneously with (i) 100 mu g of **antibody** B5, directed against Neisseria inner core **LPS** and (ii) N. meningitidis MC58 (a **galE** mutant). After 24 hours, bacteremia was 300/ml, compared with 5000/ml in untreated controls.

USE - (A) are used to treat meningitis, septicemia, pneumonia etc. associated with N. **meningitidis**, especially **group B** and urethritis, salpingitis associated with N. **gonorrhoeae**. **Antibodies** reactive with (I) can be used similarly (passive immunization).

ADVANTAGE - Inner core epitopes are common to many clinical

isolates of a particular species, so only a few (2-6) will be required to protect against all strains.
Dwg.0/5

L25 ANSWER 5 OF 27 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001231775 EMBASE
TITLE: Molecular mimicry of host structures by **lipooligosaccharides** of Neisseria meningitidis: Characterization of sialylated and nonsialylated lacto-N-neotetraose (Galβ1-4GlcNacβ1-3Galβ1-4Glc) structures in **lipooligosaccharides** using monoclonal **antibodies** and specific lectins.
AUTHOR: Tsai C.-M.
CORPORATE SOURCE: C.-M. Tsai, Division of Bacterial Products, Ctr. for Biologics Evaluation/Res., FDA, Bethesda, MD 20892, United States
SOURCE: Advances in Experimental Medicine and Biology, (2001) 491/- (525-542).
Refs: 79
ISSN: 0065-2598 CODEN: AEMBAP
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Neisseria meningitidis** **lipooligosaccharides** (LOSs) are classified into 12 immunotypes. Most LOSs are heterogeneous in having a few components by SDS-PAGE analysis that differ antigenically and chemically. We have utilized a monoclonal **antibody** that recognizes lacto-N-neotetraose (LNnT) and the lectin, Maackia amurensis leukoagglutinin (MAL), which is specific for NeuNAcα2-3Galβ1-4GlcNAc trisacchride sequence to characterize the 12 N. **meningitidis** LOSs. Using the combination of ELISA, SDS-PAGE, Western blotting, and other chemical analyses, we have shown that the LNnT (Galβ1-4GlcNAcβ1-3Galβ1-4Glc) sequence was present in the 4.0-kDa **LOS** components of seven immunotype LOSs seen on SDS-PAGE. Six of the seven LNnT-containing LOSs also bound the MAL lectin indicating that N-acetylneuraminic acid (NeuNAc) was α2,3-linked to the LNnT sequence in the LOSs. Sialylation of the terminal Gal of LNnT-containing 4.0-kDa component caused only a slight increase in its apparent MW to 4100 on SDS-PAGE. The one **LOS** with the LNnT-containing component, but not MAL-binding, was from a Group A N. **meningitidis**, which does not synthesize CMP-NeuNAc, the substrate needed for **LOS** sialylation. Thus, it is concluded (1) a common LNnT sequence is present in seven immunotype LOSs in addition to their immunotype epitopes, and (2) NeuNAc is α2->3 linked to the terminal Gal of LNnT if a organism synthesizes CMP-NeuNAc such as **Groups B** and C organisms. The above conclusions are consistent with the published structures of N. **meningitidis** LOSs. The results also demonstrate that

specific carbohydrate-binding lectins and monoclonal **antibodies** can be used as simple yet effective tools to characterize specific carbohydrate sequences in a bacterial **LOS** or **LPS** such as N. **meningitidis** **LOS**. It is intriguing that N. **meningitidis** LOSs mimic certain glycosphingolipids, such as paragloboside (LNnT-ceramide) and sialylparagloboside, and some glycoproteins of the host in having LNnT and N-acetyllactosamine sequences respectively with or without α2->3 linked NeuNAc. Epidemiological studies of N. **meningitidis** suggest that the molecular mimicry of host structures by its **LOS** plays a role in the **pathogenesis** of N. **meningitidis** by helping the organism to evade host immune defenses in man. The molecular mimicry of host structures by **LOS** or **LPS** is also found in other human **pathogens** such as N. **gonorrhoeae**, Haemophilus ducreyi, H. influenaze, Moraxella catarrhalis, Campylobacter jejuni, and Helicobacter pylori.

L25 ANSWER 6 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-679490 [66] WPIDS
CROSS REFERENCE: 2000-679491 [66]
DOC. NO. CPI: C2000-206639
TITLE: Immunogenic compositions useful as vaccines comprise a recombinant protein of toxin A or B of Clostridium difficile conjugated to a polysaccharide of a microbial pathogen.
DERWENT CLASS: B04 D16
INVENTOR(S): LYLERLY, D M; MONCRIEF, J S; PAVLIAKOVA, D; ROBBINS, J B; SCHEERSON, R; WILKINS, T D
PATENT ASSIGNEE(S): (TECH-N) TECHLAB INC; (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000061761	A2	20001019	(200066)*	EN	45
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000043372	A	20001114	(200108)		
EP 1165796	A2	20020102	(200209)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002541808	W	20021210	(200301)		53

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000061761	A2	WO 2000-US9523	20000410
AU 2000043372	A	AU 2000-43372	20000410
EP 1165796	A2	EP 2000-923206	20000410

			WO 2000-US9523	20000410
JP 2002541808	W		JP 2000-611684	20000410
			WO 2000-US9523	20000410

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000043372	A	Based on	WO 2000061761
EP 1165796	A2	Based on	WO 2000061761
JP 2002541808	W	Based on	WO 2000061761

PRIORITY APPLN. INFO: US 2000-186201P 20000301; US 1999-128686P 19990409

AN 2000-679490 [66] WPIDS

CR 2000-679491 [66]

AB WO 200061761 A UPAB: 20030101

NOVELTY - An immunogenic composition (I) comprising a recombinant protein (RP) and a polysaccharide component (PC), in which the protein is encoded by a gene from a strain of Clostridium difficile and PC is isolated from a strain of pathogenic microorganism or is chemically synthesized.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparation of (I);

(2) a recombinant genetic sequence (II) comprising a gene encoding a protein from a strain of C. difficile;

(3) an expression vector (III) comprising (II) and a gene that confers a selective phenotype upon a microbial host;

(4) a microbial host transformed with (III);

(5) use of (I) for the production of **antibodies** for passive immunotherapy against a pathogenic microorganism; and (6) a vaccine (IV) comprising (I).

ACTIVITY - T-cell dependent or **antibody** responses elicitor.

MECHANISM OF ACTION - Vaccine. The biological activity of (I) was tested in mice. Female 5 weeks-old Swiss Albino mice were injected subcutaneously with 0.1 ml containing 2.5 micro g polysaccharide in the conjugate every 2 weeks. Mice were exsanguinated 2 weeks after the first injection and 1 week after the second and third injections. IgG and IgM **antibodies** to S. flexneri type 2a **LPS** and E. coli K1 polysaccharides were measured by ELISA. IgG anti-pneumococcal type 14 polysaccharide were assayed by ELISA and total polysaccharide **antibody** by radioimmunoassay (RIA). Both conjugates, Pn14-rARU and Pn14-rARUscucc elicited statistically significant rises of IgG **antibodies** after the first and second injections. Immune responses were also significant for both, S. flexneri SF-rARU and SF-rARUsucc and E. coli K1-rARUsucc.

USE - (I) is useful for eliciting a protective immune response (T-cell dependent or T-cell independent, a cellular or humoral immune response) to a strain of **pathogenic** microorganism such as Streptococcus pneumoniae of serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, (preferably) 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 25 and 33F, **Neisseria meningitidis** serogroup B, Escherichia coli K1 and Shigella flexneri serotype 2a,

which produce the polysaccharide in vivo, in a mammal. The immunogenic composition also elicits a protective immune response against the polysaccharide produced by a strain of a nosocomial **pathogenic** microorganism such as Staphylococcus aureus serogroup 5 or 8, coagulase-negative Staphylococcus, Enterococcus sp., Enterobacter sp., Candida sp., **group B** Streptococcus, E. coli or Pseudomonas sp.. The immunogenic compositions are useful as vaccines for humans, particularly children and animals (claimed) in affording protection against one or more microbial **pathogens**.

DESCRIPTION OF DRAWING(S) - The figure shows the Clostridium difficile toxins A and B.

Dwg.1/6

L25 ANSWER 7 OF 27 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-514762 [46] WPIDS
DOC. NO. CPI: C2000-153563
TITLE: A transdermal vaccine for inducing a protective or tolerogenic immune response on human or animal skin comprises a transdermal carrier, a compound which specifically releases or induces (anti-) cytokine activity and an antigen or allergen.
DERWENT CLASS: B04 B07 C06 D16
INVENTOR(S): CEVC, G; CHOPRA, A
PATENT ASSIGNEE(S): (IDEA-N) IDEA AG
COUNTRY COUNT: 34
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000044349	A1	20000803	(200046)*	EN	79
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU BR CA CN HU JP KR MX US					
EP 1031346	A1	20000830	(200047)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 2000027988	A	20000818	(200057)		
EP 1146858	A1	20011024	(200171)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
BR 2000007749	A	20011113	(200201)		
EP 1031346	B1	20020502	(200230)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
KR 2001112252	A	20011220	(200239)		
DE 69901377	E	20020606	(200245)		
CN 1342066	A	20020327	(200247)		
HU 2002000315	B	20020528	(200249)		
ES 2173678	T3	20021016	(200279)		
JP 2002535350	W	20021022	(200301)		93
MX 2001007657	A1	20030601	(200417)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000044349	A1	WO 2000-EP597	20000126

EP 1031346	A1	EP 1999-101479	19990127
AU 2000027988	A	AU 2000-27988	20000126
EP 1146858	A1	EP 2000-906231	20000126
		WO 2000-EP597	20000126
BR 2000007749	A	BR 2000-7749	20000126
		WO 2000-EP597	20000126
EP 1031346	B1	EP 1999-101479	19990127
KR 2001112252	A	KR 2001-709479	20010727
DE 69901377	E	DE 1999-601377	19990127
		EP 1999-101479	19990127
CN 1342066	A	CN 2000-804453	20000126
HU 2002000315	B	WO 2000-EP597	20000126
		HU 2002-315	20000126
ES 2173678	T3	EP 1999-101479	19990127
JP 2002535350	W	JP 2000-595653	20000126
		WO 2000-EP597	20000126
MX 2001007657	A1	WO 2000-EP597	20000126
		MX 2001-7657	20010727

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000027988	A	Based on	WO 2000044349
EP 1146858	A1	Based on	WO 2000044349
BR 2000007749	A	Based on	WO 2000044349
DE 69901377	E	Based on	EP 1031346
HU 2002000315	B	Based on	WO 2000044349
ES 2173678	T3	Based on	EP 1031346
JP 2002535350	W	Based on	WO 2000044349
MX 2001007657	A1	Based on	WO 2000044349

PRIORITY APPLN. INFO: EP 1999-101479 19990127
AN 2000-514762 [46] WPIDS
AB WO 200044349 A UPAB: 20000921
NOVELTY - A transdermal vaccine (I) comprising a transdermal carrier, a compound which specifically releases or induces (anti-) cytokine activity and a (mixture of) antigen or allergen, is new.

DETAILED DESCRIPTION - A transdermal vaccine comprises:

(a) a transdermal carrier;

(b) a compound which specifically releases or induces cytokine or anti-cytokine activity or exerts such an activity itself; and

(c) a (mixture of) antigen or allergen.

The transdermal carrier is a penetrant, suspended or dispersed in an aqueous solvent, in the form of a minute fluid droplet surrounded by a membrane like coating of one or several layers of at least two different substances or two different forms of a substance with the tendency to aggregate. The substances differ by at least a factor of 10 in solubility in a preferably aqueous , liquid medium, so that the average diameter of homoaggregates of the more soluble substances or heteroaggregates of both substances is smaller than the average diameter of the homoaggregates of the less soluble substance. The more soluble component tends to solubilize the penetrating droplet. The content of this component amounts to up to 99 mol-% of the concentration required to solubilize the droplet, or to 99 mol-% of the saturating concentration in the unsolubilized

droplet, whichever is highest. The elastic deformation energy of the droplet surrounding the membrane like coating is at least 5 multiply lower, more preferably more than 10 multiply lower than that of the red blood cells or of the phospholipid bilayer with fluid aliphatic chains.

INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising, in a bottled or otherwise packaged form, at least one dose of (I); and

(2) generating a protective immune response on a mammal with (I).

ACTIVITY - Immunostimulant.

No supporting biological data given.

MECHANISM OF ACTION - Vaccine.

No supporting biological data given.

USE - For inducing a protective or tolerogenic immune response on human or animal skin (claimed).

ADVANTAGE - The vaccine provides immunization without local irritation.

Dwg.0/14

L25 ANSWER 8 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 2

ACCESSION NUMBER: 2002:440050 BIOSIS
DOCUMENT NUMBER: PREV200200440050
TITLE: Gene expression and production of tumor necrosis factor alpha, interleukin-1beta (IL-1beta), IL-8, macrophage inflammatory protein 1alpha (MIP-1alpha), MIP-1beta, and gamma interferon-inducible protein 10 by human neutrophils stimulated with **group B meningococcal** outer membrane vesicles.
AUTHOR(S): Lapinet, Jose A.; Scapini, Patrizia; Calzetti, Federica; Perez, Oliver; Cassatella, Marco A. [Reprint author]
CORPORATE SOURCE: Department of Pathology, Section of General Pathology, Strada Le Grazie 4, I-37134, Verona, Italy MCNCSS@borgoroma.univr.it
SOURCE: Infection and Immunity, (December, 2000) Vol. 68, No. 12, pp. 6917-6923. print.
CODEN: INFIBR. ISSN: 0019-9567.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Aug 2002
Last Updated on STN: 14 Aug 2002

AB Accumulation of polymorphonuclear neutrophils (PMN) into the subarachnoidal space is one of the hallmarks of Neisseria meningitidis infection. In this study, we evaluated the ability of outer membrane vesicles (OMV) from N. meningitidis B to stimulate cytokine production by neutrophils. We found that PMN stimulated in vitro by OMV produce proinflammatory cytokines and chemokines including tumor necrosis factor alpha (TNF-alpha), interleukin-1beta (IL-1beta), IL-8, macrophage inflammatory protein 1alpha (MIP-1alpha), and MIP-1beta. A considerable induction of gamma interferon (IFN-gamma) inducible protein 10 (IP-10) mRNA transcripts, as well as extracellular IP-10 release, was also observed when neutrophils were stimulated by OMV in combination with

IFN-gamma. Furthermore, PMN stimulated by OMV in the presence of IFN-gamma demonstrated an enhanced capacity to release TNF-alpha, IL-1beta, IL-8, and MIP-1beta compared to stimulation with OMV alone. In line with its down-regulatory effects on neutrophil-derived proinflammatory cytokines, IL-10 potently inhibited TNF-alpha, IL-1beta, IL-8, and MIP-1beta production triggered by OMV. Finally, a neutralizing anti-TNF-alpha monoclonal **antibody** (MAb) did not influence the release of IL-8 and MIP-1beta induced by OMV, therefore excluding a role for endogenous TNF-alpha in mediating the induction of chemokine release by OMV. In contrast, the ability of **lipopolysaccharide** from N. meningitidis B to induce the production of IL-8 and MIP-1beta was significantly inhibited by anti-TNF-alpha MAb. Our results establish that, in response to OMV, neutrophils produce a proinflammatory profile of cytokines and chemokines which may not only play a role in the pathogenesis of meningitis but may also contribute to the development of protective immunity to serogroup B meningococci.

L25 ANSWER 9 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1999:446826 BIOSIS
DOCUMENT NUMBER: PREV199900446826
TITLE: Immunization with **meningococcal** outer-membrane protein vesicles containing **lipooligosaccharide** protects mice against lethal experimental **group B** **Neisseria meningitidis** infection and septic shock.
AUTHOR(S): Quakyi, Emmanuel K.; Frasch, Carl E.; Buller, Nicole; Tsai, Chao-Ming [Reprint author]
CORPORATE SOURCE: Division of Bacterial Products, Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD, 20892, USA
SOURCE: Journal of Infectious Diseases, (Sept., 1999) Vol. 180, No. 3, pp. 747-754. print.
CODEN: JIDIAQ. ISSN: 0022-1899.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Oct 1999
Last Updated on STN: 26 Oct 1999

AB Detergent-treated **group B Neisseria** **meningitidis** outer membrane vesicles (D-OMVs) from wild-type M986 and from nonencapsulated mutant M986-non-capsule variant (NCV) were compared as immunogens. Eight weeks after 3 consecutive immunizations with the immunogens, mice were challenged with a lethal dose of purified **endotoxin** or heat-killed or living N. meningitidis, plus D-galactosamine (400 mg/kg). D-OMVs from M986 induced bactericidal **antibodies** to both M986 (B:2a:P1.5,2:L3,7) and 6275 (B:2a:P1.2,5:L3) and protected the animals against both strains, whereas D-OMVs from M986-NCV did not protect the animals against infection with 6275 even when high serum bactericidal activity was induced. Tumor necrosis factor-alpha detected after bacterial infection was high in both protected and unprotected mice; interleukin (IL)-6 was high in mice that died but

10/089583

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Set Items Description
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-key terms

Set Items Description
S1 934 (NEISSER? OR MENINGITID? OR MENINGOCOCC?)(10N)((TYPE OR SEROTYPE OR GROUP)(1N)B)
S2 171 S1 AND (PATHOGEN?(5N)NEISSER? OR GONORRHOEAE OR GONOCOCC?)

S6 6 S2 AND (GALE OR GAL(W)E)
S7 70 S2 AND (LPS OR LOS OR LIPOOLIGOSACCHARIDE? ? OR LIPOPOLYSACCHARIDE? ? OR LIPO(W)(POLYSACCHARIDE? ? OR OLIGOSACCHARIDE? ? OR (POLY OR OLIGO)(W)SACCHARIDE? ?) OR (LIPOPOLY OR LIPOOLIGO)(W)SACCHARIDE? ? OR ENDOTOXIN? ?)
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S9 55 S6 OR S8
S10 39 RD (unique items)
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10/3,AB/1 (Item 1 from file: 65)
DIALOG(R)File 65:Inside Conferences
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03897822 INSIDE CONFERENCE ITEM ID: CN040960594
Functional studies of **antibodies** to inner core **lipopolysaccharide** (**LPS**) of **Neisseria meningitidis** (Nm) **group B**, using a flow cytometric -based opsonophagocytosis assay
Plested, J. S.; Ferry, B. F.; Lehmann, A. K.; Makepeace, K.; Griffiths, H. G.; Bird, A. G.; Moxon, E. R.
CONFERENCE: International pathogenic Neisseria conference-11th
ABSTRACTS OF THE INTERNATIONAL PATHOGENIC NEISSERIA CONFERENCE , 1998; 11TH P: 296
Paris, EDK, 1998
ISBN: 2842540158
LANGUAGE: English DOCUMENT TYPE: Conference Selected abstracts
CONFERENCE LOCATION: Nice, France 1998; Nov (199811) (199811)

10/3,AB/2 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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15445448 Document Delivery Available: 000180406700043 References: 37
TITLE: Nonencapsulated Neisseria meningitidis strain produces amylopectin from sucrose: Altering the concept for differentiation between N-meningitidis and N. polysaccharea
AUTHOR(S): Zhu PX (REPRINT); Tsang RSW; Tsai CM
AUTHOR(S) E-MAIL: Zhu@cber.fda.gov
CORPORATE SOURCE: US FDA, Div Bacterial Parasit & Allergen Prod, 8800 Rockville Pike/Bethesda//MD/20892 (REPRINT); US FDA, Div Bacterial Parasit & Allergen Prod, /Bethesda//MD/20892
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 2003, V41, N1 (JAN), P 273-278
GENUINE ARTICLE#: 635NY
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0095-1137
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Neisseria meningitidis is the causative agent of meningococcal sepsis and meningitis. Neisseria polysaccharea is a nonpathogenic species. N. polysaccharea is able to use sucrose to produce amylopectin, a starch-like polysaccharide, which distinguishes it biochemically from the pathogenic species N. meningitidis. The data presented here indicate that this may be an insufficient criterion to distinguish between these two species. The nonencapsulated Neisseria strain 93246 expressed a phenotype of amylopectin production similar to that of N. polysaccharea. However, strain 93246 reacted with N. meningitidis serotype 4 and serosubtype P1.14 monoclonal **antibodies** and showed the N. meningitidis L1(8) **lipo -oligosaccharide** immunotype. Further analyses were performed on four genetic loci in strain 93246, and the results were compared with 7 N. meningitidis strains, 13 N. polysaccharea strains, and 2 N. **gonorrhoeae** strains. Three genetic loci, opcA, siaD, and lgt-1 in strain 93246, were the same as in N. meningitidis. Particularly, the siaD gene encoding polysialyltransferase responsible for biosynthesis of N. **meningitidis group B** capsule was detected in strain 93246. This siaD gene was inactivated by a frameshift mutation at the poly(C) tract, which makes strain 93246 identical to other nonencapsulated N. meningitidis strains. As expected, the ants gene encoding amylosucrase, responsible for production of amylopectin from sucrose, was detected in strain 93246 and all 13 N. polysaccharea strains but not in N. meningitidis and N. **gonorrhoeae** strains. These data suggest that strain 93246 is nonencapsulated N. meningitidis but has the ability to produce extracellular amylopectin from sucrose. The gene for amylopectin production in strain 93246 was likely imported from N. polysaccharea by horizontal genetic exchange. Therefore, we conclude that genetic analysis is required to complement the traditional phenotypic classification for the nonencapsulated Neisseria strains.

10/3,AB/3 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

14780604 Document Delivery Available: 000178270300002 References: 32
TITLE: Structural analysis of the **lipopolysaccharide** from Neisseria

meningitidis strain BZ157 **galE**: localisation of two phosphoethanolamine residues in the inner core oligosaccharide
AUTHOR(S): Cox AD (REPRINT); Li JJ; Brisson JR; Moxon ER; Richards JC
AUTHOR(S) E-MAIL: andrew.cox@nrc.ca
CORPORATE SOURCE: Natl Res Council Canada, Inst Biol Sci, 100 Sussex Dr,Rm 3089/Ottawa/ON K1A 0R6/Canada/ (REPRINT); Natl Res Council Canada, Inst Biol Sci, /Ottawa/ON K1A 0R6/Canada/; Univ Oxford, Inst Mol Med, /Oxford OX3 9DU//England/
PUBLICATION TYPE: JOURNAL
PUBLICATION: CARBOHYDRATE RESEARCH, 2002, V337, N16 (SEP 9), P1435-1444
GENUINE ARTICLE#: 598HN
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0008-6215
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The structure of the phase-variable **lipopolysaccharide** (**LPS**) from the **group B Neisseria meningitidis** strain BZ157 **galE** was elucidated. The structural basis for the **LPS**'s variation in reactivity with a monoclonal **antibody** (MAb) B5 that has specificity for the presence of phosphoethanolamine (PEtn) at the 3-position of the distal heptose residue (HepII) was established. The structure of the O-deacylated **LPS** was deduced by a combination of monosaccharide analyses, nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry. These analyses revealed the presence of a novel inner core oligosaccharide (OS) structure in the MAb B5 reactive (B5 +) **LPS** that contained two PEtn residues simultaneously substituting the 3- and 6-positions of the HepII residue. The determination of this structure has identified a further degree of variability within the inner core OS of meningococcal **LPS** that could contribute to the interaction of meningococcal strains with their host.

10/3,AB/4 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10323249 References: 43
TITLE: Effect of normal and immune sera on Haemophilus ducreyi 35000HP and its isogenic MOMP and **LOS** mutants
AUTHOR(S): Hiltke TJ; Bauer ME; Klesney-Tait J; Hansen EJ; Munson RS; Spinola SM (REPRINT)
CORPORATE SOURCE: Indiana Univ, Dept Immunol & Microbiol, 435 Emerson Hall,545 Barnhill Dr/Indianapolis//IN/46202 (REPRINT); Indiana Univ, Dept Immunol & Microbiol, /Indianapolis//IN/46202; Indiana Univ, Dept Med, /Indianapolis//IN/46202; Indiana Univ, Dept Pathol & Lab Med, /Indianapolis//IN/46202; Univ Texas, Dept Microbiol, /Dallas//TX/; Childrens Hosp Res Fdn, /Columbus//OH/; Ohio State Univ, Dept Pediat, /Columbus//OH/43210; Ohio State Univ, Dept Immunol & Med Microbiol, /Columbus//OH/43210
PUBLICATION TYPE: JOURNAL
PUBLICATION: MICROBIAL PATHOGENESIS, 1999, V26, N2 (FEB), P93-102
GENUINE ARTICLE#: 170TA
PUBLISHER: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND
ISSN: 0882-4010

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: A bactericidal assay was developed in order to test the effect of hyperimmune rabbit sera on the viability of serum-resistant Haemophilus ducreyi 35000HP. Testing of several lots of rabbit complement and time course experiments showed that the serum-sensitive H. ducreyi CIPA77 was killed efficiently by 25% complement at 35 degrees C in 3 h. We hypothesized that incubation of 35000HP under these conditions with the appropriate bactericidal **antibody** would kill this strain. A panel of high titre rabbit antisera was developed and tested against 35000HP. The panel included antisera raised to whole cells, total membranes, Sarkosyl-insoluble outer membrane proteins, the H. ducreyi lipoprotein, and the peptidoglycan-associated lipoprotein. None of the antisera convincingly showed bactericidal activity. The bactericidal assay was also used to determine the effect of normal human serum (NHS) on isogenic mutants of 35000HP. 35000HP-RSM2, an Omega kan insertion mutant that expresses a truncated **lipooligosaccharide**, was as resistant to NHS as its parent. A mutant deficient in expression of the major outer membrane protein (35000.60) was sensitive to NHS. We conclude that 35000HP is relatively resistant to normal and hyperimmune sera, and that the major outer membrane protein contributes to this resistance. (C) 1999 Academic Press.

10/3,AB/5 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08855226 References: 54
TITLE: Complement factor C3 deposition and serum resistance in isogenic capsule and **lipooligosaccharide** sialic acid mutants of serogroup B Neisseria meningitidis
AUTHOR(S): Vogel U (REPRINT); Weinberger A; Frank R; Muller A; Kohl J; Atkinson JP; Frosch M
CORPORATE SOURCE: UNIV WURZBURG,INST HYG & MIKROBIOL, JOSEF SCHNEIDER STR 2/D-97080 WURZBURG//GERMANY/ (REPRINT); HANNOVER MED SCH,INST MED MIKROBIOL/D-30625 HANNOVER//GERMANY/; GESELL BIOTECHNOL FORSCH MBH,/D-38124 BRAUNSCHWEIG//GERMANY/; WASHINGTON UNIV,SCH MED, DEPT MED/ST LOUIS//MO/63110
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1997, V65, N10 (OCT), P4022-4029
GENUINE ARTICLE#: XY522
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Serogroup B meningococci express sialic acids on their surfaces as a modification of the **lipooligosaccharide** (**LOS**) and as capsular material consisting of alpha 2,8-linked sialic acid homopolymers. The aim of this study was to elucidate the impact of each sialic acid component on the deposition of complement factor C3 and serum resistance, For this purpose, we used isogenic mutants deficient in capsule expression (a polysialyltransferase mutant) or sialylation of the **LOS** (a **galE** mutant) or both (a mutant with a deletion of the cps gene locus). Bactericidal assays using 40% normal human serum (NHS) demonstrated that both the capsule and **LOS** sialic acid are indispensable for serum

resistance. By immunoblotting with monoclonal **antibody** MAb755 that is specific for the C3 alpha-chain, we were able to demonstrate that C3 from 40% NHS was covalently linked to the surface structures of meningococci as C3b and iC3b, irrespective of the surface sialic acid compounds, However, C3b linkage was more pronounced and occurred on a larger number of target molecules in **galE** mutants with nonsialylated **LOS** than in meningococci with mild-type **LOS**, irrespective of the capsule phenotype. C3b deposition was caused by both the classical pathway (CP) and the alternative pathway of complement activation. Use of 10% NHS revealed that at low serum concentrations, C3 deposition occurred via the CP and was detected primarily on nonsialylated-**LOS galE** mutants, irrespective of the capsular phenotype. Accordingly, immunoglobulin M (IgM) binding to meningococci from heat-inactivated NHS was demonstrated only in both encapsulated and unencapsulated **galE** mutants. In contrast, inhibition of IgA binding required both encapsulation and **LOS** sialylation. We conclude that serum resistance in wild-**type** serogroup **B meningococci** can only be partly explained by an alteration of the C3b linkage pattern, which seems to depend primarily on the presence of wild-type **LOS**, since a serum-resistant phenotype also requires capsule expression.

10/3,AB/6 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08206840 References: 58
TITLE: Outer membrane proteins of bovine Pasteurella multocida serogroup A isolates
AUTHOR(S): Dabo SM (REPRINT); Confer AW; Murphy GL
CORPORATE SOURCE: OKLAHOMA STATE UNIV,COLL VET MED, DEPT ANAT PATHOL & PHARMACOL/STILLWATER//OK/74078 (REPRINT)
PUBLICATION TYPE: JOURNAL
PUBLICATION: VETERINARY MICROBIOLOGY, 1997, V54, N2 (FEB), P167-183
GENUINE ARTICLE#: WJ620
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
ISSN: 0378-1135
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The outer membrane proteins (OMPs) of P. multocida serotypes A3 (7 isolates), A4 (2 isolates), A3,4 and A2 (one isolate each) obtained from pneumonic cattle (10 isolates) and from one pig isolate were investigated to identify potential immunogens. SDS-PAGE of P. multocida OM isolated by SDG centrifugation of spheroplasts revealed eight major OMPs. Outer membranes isolated by sarcosyl extraction or SDG had similar protein composition on Coomassie blue-stained SDS-PA gel and on immunoblots. Two major OMPs (M(r)s of 35 and 46 kDa at 100 degrees C) demonstrated heat modifiability with apparent M(r)s of 30 and 34 kDa at 37 degrees C, respectively. The N-terminal aa sequences of these heat modifiable proteins revealed homology with E. coli OmpA and Hib P1 proteins, respectively. Protease treatment of whole cells followed by western immunoblots using bovine convalescent sera identified several immunogenic, surface-exposed and conserved OMPs among the eleven P. multocida isolates examined. The whole organism SDS-PAGE profiles of the eleven P. multocida isolates differed such that six patterns were seen. These patterns could potentially be used as a typing system for P. multocida bovine isolates based on the

molecular weights of whole cell proteins. The above observations have potentially important implications relative to the immunity to infection.

10/3,AB/7 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07932570 References: 51
TITLE: Mesophilic Aeromonas sp serogroup 0:11 resistance to complement-mediated killing
AUTHOR(S): Merino S; Rubires X; Aguilar A; Alberti S; HernandezAlles S; Benedi VJ; Tomas JM
CORPORATE SOURCE: UNIV BARCELONA,DEPT MICROBIOL, DIAGONAL 645/E-08071 BARCELONA//SPAIN/ (REPRINT); UNIV BARCELONA,DEPT MICROBIOL/E-08071 BARCELONA//SPAIN/; UNIV BALEARIC ISL,DEPT BIOL AMBIENTALE, MICROBIOL LAB/PALMA DE MALLORCA//SPAIN/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 1996, V64, N12 (DEC), P5302-5309
GENUINE ARTICLE#: VU635
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The complement activation by and resistance to complement-mediated killingof Aeromonas sp. strains from serogroup O:11 were investigated by using different wild-type strains (with an S-layer characteristic of this serogroup) and their isogenic mutants characterized for their surface components (S-layer and **lipopolysaccharide** [**LPS**]). All of the Aeromonas sp. serogroup O:11 wild-type strains are unable to activate complement, which suggested thatthe S-layer completely covered the **LPS** molecules. We found that the classical complement pathway is involved in serum killing of susceptible Aeromonas sp. mutant strains of serogroup O11, while the alternative complement pathway: seems not to be involved, and that the complement activation seems tobe independent of **antibody**. The smooth mutant strains devoid of the S-layer (S-layer isogenic mutants) or isogenic **LPS** mutant strains with a completeor rather complete **LPS** core (also without the S-layer) are able to activate complement but are resistant to complement-mediated killing. The reasons for this resistance are that C3b is rapidly degraded, and therefore the lgtic membrane attack complex (C5b-9) is not formed. Isogenic **LPS** rough mutants with an incomplete **LPS** core are serum sensitive because they bind more C3b than the resistant strains, the C3b is not completely degraded, and therefore the lytic complex (C5b-9) is formed.

10/3,AB/8 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07023605 References: 32
TITLE: DETECTION OF STRAIN-SPECIFIC ANTIGENIC EPITOPES ON THE **LIPO-OLIGOSACCHARIDE** OF HAEMOPHILUS PARASUIS BY USE OF MONOCLONAL AND POLYCLONAL **ANTIBODIES**

AUTHOR(S): ZUCKER BA; BAGHIAN A; TRUAX R; OREILLY KL; STORZ J (Reprint)
CORPORATE SOURCE: LOUISIANA STATE UNIV,SCH VET MED,DEPT VET MICROBIOL & PARASITOL/BATON ROUGE//LA/70803 (Reprint); LOUISIANA STATE UNIV,SCH VET MED,DEPT VET MICROBIOL & PARASITOL/BATON ROUGE//LA/70803
PUBLICATION: AMERICAN JOURNAL OF VETERINARY RESEARCH, 1996, V57, N1 (JAN), P63-67
GENUINE ARTICLE#: TN538
ISSN: 0002-9645
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Objective-To investigate the antigenic diversity of **lipooligosaccharides** of Haemophilus parasuis.

Procedures-Immunoblot assays were done with monoclonal and polyclonal **antibodies** on whole-cell lysates. individual colonies of H parasuis strains H 54, H 53, and H 128 were tested for reactivity with **lipo-oligosaccharide**-specific monoclonal **antibodies** after a single passage on chocolate agar, and colonies of strain H 54 were analyzed after 10 passages. Colony blot tests were used to screen H parasuis strains for spontaneously occurring antigenic variation in their **lipo-oligosaccharides**.

Results-Eight H parasuis strains were separated into 4 **lipo-oligosaccharide** serovars on the basis of immunoblot reactions with 3 polyclonal rabbit antisera. Nine monoclonal **antibodies** against **lipo-oligosaccharides** of a **lipo-oligosaccharide** -serovar I strain reacted with all tested serovar I strains but failed to react with other H parasuis strains.

Conclusions-Variations in the antigenic reactivity after 1 or 10 passages on chocolate agar were not observed. The serovar I **lipo-oligosaccharide** strains included virulent as well as avirulent H parasuis strains, indicating that these epitopes do not correlate directly with virulence properties of H parasuis.

10/3,AB/9 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

06393844 References: 48
TITLE: INVESTIGATIONS INTO THE MOLECULAR BASIS OF MENINGOCOCCAL TOXICITY FOR HUMAN ENDOTHELIAL AND EPITHELIAL CELLS - THE SYNERGISTIC EFFECT OF **LPS** AND PILI
AUTHOR(S): DUNN KLR; VIRJI M (Reprint); MOXON ER
CORPORATE SOURCE: UNIV OXFORD,JOHN RADCLIFFE HOSP,DEPT PAEDIAT/OXFORD OX3 9DU//ENGLAND/ (Reprint); UNIV OXFORD,JOHN RADCLIFFE HOSP,DEPT PAEDIAT/OXFORD OX3 9DU//ENGLAND/
PUBLICATION: MICROBIAL PATHOGENESIS, 1995, V18, N2 (FEB), P81-96
GENUINE ARTICLE#: QX649
ISSN: 0882-4010
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Using human umbilical vein endothelial cells as an in vitro model of toxicity, it was found that Neisseria meningitidis, Neisseria **gonorrhoeae**, Neisseria lactamica and Neisseria sicca caused damage to

these cells, in contrast to the lack of cytotoxicity exhibited by Haemophilus influenzae **type b**. N. **meningitidis** was also found to be toxic for human epithelial cells. The major toxic factor of N, meningitidis was found to be a heat-stable component of outer membrane vesicles, and could be inhibited by polymyxin B, suggesting that **lipopolysaccharide** plays a major role in toxicity. However, the toxicity mediated by **lipopolysaccharide** was modulated significantly by pilus-dependent adherence. Intra-strain variants expressing altered pilins which exhibited different levels of adherence to epithelial and endothelial cells were used to study the role of pilus. The degree of toxicity observed correlated with their relative level of adherence to cultured cells. In contrast, Ope-dependent increased adherence did not result in increased toxicity for endothelial cells, suggesting that pill have a synergistic effect, contributing to the overall damage.

10/3,AB/10 (Item 9 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05537557 References: 38
TITLE: TN916-GENERATED, **LIPOOLIGOSACCHARIDE** MUTANTS OF NEISSERIA MENINGITIDIS AND NEISSERIA **GONORRHOEAE**
AUTHOR(S): STEPHENS DS; MCALLISTER CF; ZHOU D; LEE FK; APICELLA MA
CORPORATE SOURCE: EMORY UNIV,SCH MED,DEPT MED,DIV INFECT DIS,69 BUTLER ST SE/ATLANTA//GA/30303 (Reprint); EMORY UNIV,SCH MED,DEPT MICROBIOL & IMMUNOL/ATLANTA//GA/30322; UNIV IOWA,DEPT MICROBIOL/IOWA CITY//IA/52242
PUBLICATION: INFECTION AND IMMUNITY, 1994, V62, N7 (JUL), P2947-2952
GENUINE ARTICLE#: NU014
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: A library of Tn916-generated, tetracycline-resistant (Tc-r) mutants of the **group B Neisseria meningitidis** strain NMB was screened by using monoclonal **antibodies** (MAbs) that recognize structural differences in neisserial **lipooligosaccharide** (**LOS**). The **LOS** of parental strain NMB had a relative molecular mass of 4.5 kDa, reacted with MAbs 3F11 and 6B4 but not with MAb 4C4 or 6E4, and contained a lacto-N-neotetrose unit. Two phenotypically stable mutants, SS3 and R6, altered in **LOS**, were identified by colony immunoblots, electrophoresis, and Western immunoblots. The **LOS** of mutant SS3 was 3.4 kDa and reacted with MAbs 4C4 and 6E4 but not MAb 3F11 or 6B4. The **LOS** of mutant R6 was 3.1 to 3.2 kDa and reacted with MAb 6E4 but not MAb 3F11, 6B4, or 4C4. Thus, the LOSS of the R6 and SS3 mutants were predicted to contain different truncations of the core oligosaccharide. The **LOS** phenotype of each mutant was linked to Tc-r, as determined by transformation of the parent strain with DNA from the mutant. Southern hybridizations and single-specific-primer PCR revealed in each mutant a single truncated Tn916 insertion which had lost genes required for mobilization. Tn916 mutagenesis was used to identify two distinct genetic sites in the meningococcal chromosome involved in biosynthesis of the oligosaccharide chain of **LOS** and to create genetically defined **LOS** mutants Of N. meningitidis and Neisseria **gonorrhoeae**.

10/3,AB/11 (Item 10 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

05386061 References: 50
TITLE: MENINGOCOCCAL GROUP A **LIPOOLIGOSACCHARIDES** (**LOS**) - PRELIMINARY STRUCTURAL STUDIES AND CHARACTERIZATION OF SEROTYPE-ASSOCIATED AND CONSERVED **LOS** EPITOPES
AUTHOR(S): KIM JJ; PHILLIPS NJ; GIBSON BW; GRIFFISS JM; YAMASAKI R
CORPORATE SOURCE: VET ADM MED CTR 111W1,4150 CLEMENT ST/SAN FRANCISCO//CA/94121 (Reprint); UNIV CALIF SAN FRANCISCO,CTR IMMUNOCHEM/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT LAB MED/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT PEDIAT/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT PHARMACEUT CHEM/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT MED/SAN FRANCISCO//CA/94143
PUBLICATION: INFECTION AND IMMUNITY, 1994, V62, N5 (MAY), P1566-1575
GENUINE ARTICLE#: NH313
ISSN: 0019-9567
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Structural studies indicate that the neisserial **lipooligosaccharides** (**LOS**) are composed of an oligosaccharide (OS) portion with a phosphorylated diheptose (Hep) core attached to the toxic lipid A moiety. A conserved meningococcal **LOS** epitope, defined by monoclonal **antibody** (MAb) D6A is expressed on group A and many **group B** and C **meningococci** of different **LOS** serotypes (J.J. Kim, R.E. Mandrell, H. Zhen, M.A. Apicella, J.T. Poolman, and J.M. Griffiss, Infect. Immun. 56:2631-2638, 1988). This MAb-defined D6A epitope is immunogenic in humans (M.M. Estabrook, R.E. Mandrell, M.A. Apicella, and J.M. Griffiss, Infect. Immun. 58:2204-2213, 1990; M.M. Estabrook, C.J. Baker, and J.M. Griffiss, J. Infect. Dis. 197:966-970, 1993). In this study, we characterize this important MAb-defined **LOS** epitope. Serotype L10 and L11 group A meningococcal **LOS** Here chemically modified and used to investigate what portion of the **LOS** molecule is important for expression of the conserved (D6A) epitope and serotype-associated **LOS** epitopes by use of immunoblotting techniques and selected MAbs as probes. Preliminary structural characterization of the **LOS** was also accomplished by electrospray ionization-mass spectrometry. Our results indicate the following. (i) **Antibodies** that recognize the serotype-associated or conserved **LOS** epitopes recognize the OS portion of the **LOS**. (ii) The phosphorylated diheptose core region of the OS is essential for expression of the conserved D6A epitope. (iii) The lipid portion of the molecule is important for optimum expression of the **LOS** epitopes. (iv) The proposed compositions of the O-deacylated **LOS** are consistent with the presence of a phosphorylated diheptose core and are as follows: for O-deacylated L10 **LOS**, 3Hex (hexose), 1HexNAc (N-acetylhexosamine), 2KDO (2-keto-3-deoxy-D-manno-octulosonic acid), 2Hep (heptose), 1PEA or 2PEA (phosphoethanolamine), and O-deacylated lipid A; and for O-deacylated L11 **LOS**, 2Hex, 1HexNAc, 2KDO, 2Hep, 2PEA, and O-deacylated lipid A. Because the phosphorylated diheptose core region of the **LOS** is essential for the formation of a conserved **LOS** epitope (D6A) that is immunogenic in humans, care should be taken to maintain stereochemical requirements for the expression of this conserved epitope in the design of effective, nontoxic **LOS** vaccines.

10/3,AB/12 (Item 11 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

04950297 References: 28
TITLE: CLONING AND MOLECULAR ANALYSIS OF THE **GALE** GENE OF NEISSERIA-MENINGITIDIS AND ITS ROLE IN **LIPOPOLYSACCHARIDE** BIOSYNTHESIS
AUTHOR(S): JENNINGS MP; VANDERLEY P; WILKS KE; MASKELL DJ; POOLMAN JT; MOXON ER
CORPORATE SOURCE: JOHN RADCLIFFE HOSP,INST MOLEC MED,MOLEC INFECTDIS GRP/OXFORD OX3 9DU//ENGLAND/ (Reprint); NATL INST PUBL HLTH & ENVIRONM PROTECT/BILTHOVEN THE//NETHERLANDS/
PUBLICATION: MOLECULAR MICROBIOLOGY, 1993, V10, N2 (OCT), P361-369
GENUINE ARTICLE#: MD250
ISSN: 0950-382X
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The **galE** gene from Haemophilus influenzae was used as a hybridization probe for the **galE** gene of **Neisseria meningitidis Group B**, identifying two different homologous loci. Each of the loci was cloned and nucleotide sequence analysis revealed that both loci contained sequences similar to **galE**. One contained a functional **galE** gene and mapped to the capsule biosynthetic locus. The second contained only a partial **galE**-coding sequence, which did not express a functional gene product. A **galE** mutant meningococcal strain was constructed by transformation with an inactivated **galE** gene. Analysis of the **LPS** from the **galE** mutant strain revealed an apparent reduction in molecular weight and a loss of reactivity with monoclonal **antibodies** specific for structures known to contain galactose. These results are consistent with an essential role for **galE** in the incorporation of galactose into meningococcal **lipopolysaccharide**.

10/3,AB/13 (Item 12 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

04078629 References: 45
TITLE: SIALYLATION AND HUMAN NEUTROPHIL KILLING OF GROUP-C NEISSERIA-MENINGITIDIS
AUTHOR(S): ESTABROOK MM; CHRISTOPHER NC; GRIFFISS JM; BAKER CJ; MANDRELL RE
CORPORATE SOURCE: SAN FRANCISCO GEN HOSP,1001 POTRERO AVE 6-E-6/SAN FRANCISCO//CA/94110 (Reprint); UNIV CALIF SAN FRANCISCO,VET ADM MED CTR,DEPT PEDIAT,CTR IMMUNOCHEM/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT LAB MED/SAN FRANCISCO//CA/94143; CASE WESTERN RESERVE UNIV,SCH MED,DEPT PEDIAT/CLEVELAND//OH/44106; BAYLOR COLL MED,DEPT PEDIAT MICROBIOL & IMMUNOL/HOUSTON//TX/77030
PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 1992, V166, N5 (NOV), P 1079-1088
GENUINE ARTICLE#: JV015
ISSN: 0022-1899
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: This study describes the association of **lipooligosaccharide** (**LOS**) and capsule sialylation with the survival of 25 serogroup C meningococcal strains in phagocytosis assays. Eleven strains isolated from children were of diverse protein serotypes or were nontypeable; 14 were serotype 2b:P1.2 and were isolated from children during or immediately after a focal epidemic in Texas. Degree of endogenous **LOS** sialylation and amount of sialic acid capsule were associated with each other and with susceptibility to killing by neutrophils for the non-2b:P1.2 strains. The 2b:P1.2 strains as a group had significantly greater survival in the presence of neutrophils than did the non-2b:P1.2 strains. The susceptibility of these strains to killing by neutrophils was not associated with endogenous **LOS** sialylation or amount of capsule. These data suggest that many virulent strains evade neutrophil killing, either by sialylation or another mechanism. Evasion of neutrophil killing might enhance a strain's epidemic potential.

10/3,AB/14 (Item 13 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03559305 References: 23
TITLE: **LIPOOLIGOSACCHARIDES** (**LOS**) OF SOME HAEMOPHILUS SPECIES MIMIC HUMAN GLYCOSPHINGOLIPIDS, AND SOME **LOS** ARE SIALYLATED
AUTHOR(S): MANDRELL RE; MCLAUGHLIN R; ABUKWAIK Y; LESSE A; YAMASAKI R; GIBSON B; SPINOLA SM; APICELLA MA (Reprint)
CORPORATE SOURCE: SUNY BUFFALO,DEPT MED/BUFFALO//NY/14215 (Reprint); SUNY BUFFALO,DEPT MED/BUFFALO//NY/14215; SUNY BUFFALO,DEPT MICROBIOL/BUFFALO//NY/14215; SUNY BUFFALO,DEPT PHARMACOL & THERAPEUT/BUFFALO//NY/14215; UNIV CALIF SAN FRANCISCO,CTR IMMUNOCHEM/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT LAB MED/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT PHARMACEUT CHEM/SAN FRANCISCO//CA/94143
PUBLICATION: INFECTION AND IMMUNITY, 1992, V60, N4 (APR), P1322-1328
GENUINE ARTICLE#: HK753
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: The **lipooligosaccharides** (**LOS**) of strains of Haemophilus ducreyi, Neisseria **gonorrhoeae**, Neisseria meningitidis, and Neisseria lactamica contain epitopes that are antigenically and structurally similar to carbohydrates present in human glycosphingolipids. **LOS** from strains of Haemophilus influenzae and H. influenzae biogroup aegyptius were tested for the binding of monoclonal **antibodies** (MAbs) that bind to human glycosphingolipids possessing Gal-beta-1-4GlcNAc (MAb 3F11) and Gal-alpha-1-4Gal-beta-1-4Glc (MAb anti-P(k)). In solid-phase radioimmunoassays, the **LOS** of 18 of 19 H. influenzae type b (Hib), 8 of 19 nontypeable H. influenzae, and 10 of 20 H. influenzae biogroup aegyptius strains bound MAb anti-P(k). The **LOS** of 13 of 19 Hib, 10 of 16 nontypeable H. influenzae, and 2 of 18 H. influenzae biogroup aegyptius strains bound MAb 3F11. Neuraminidase treatment of the strains increased the binding of MAb 3F11 by more than twofold in 47% of the H. influenzae strains, suggesting that sialic acid occluded the **LOS** structure recognized by MAb 3F11. The material released from neuraminidase-treated Hib **LOS** was confirmed to be sialic acid by high-performance anion-exchange chromatography. A recombinant plasmid

containing genes involved in Hib **LOS** biosynthesis directed the expression (assembly) of the 3F11 epitope in Escherichia coli. These studies demonstrate that H. influenzae and H. influenzae biogroup aegyptius express at least two **LOS** epitopes that are similar to those present in human glycosphingolipids. Sialic acid was present on the **LOS** of some H. influenzae strains and prevented the binding of MAb 3F11 to its epitope. The oligosaccharide portion of sialylated **LOS** may also resemble sialylated oligosaccharides present in human glycosphingolipids (gangliosides).

10/3,AB/15 (Item 14 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

03123017 References: 31
TITLE: T-CELL RECOGNITION OF NEISSERIA-MENINGITIDIS CLASS-1 OUTER MEMBRANE PROTEINS - IDENTIFICATION OF T-CELL EPITOPES WITH SELECTED SYNTHETIC PEPTIDES AND DETERMINATION OF HLA RESTRICTION ELEMENTS
AUTHOR(S): WIERTZ EJHJ; VANGAANSVANDENBRINK JAM; SCHREUDER GMTH; TERMIJTELEN AAM; HOOGERHOUT P; POOLMAN JT
CORPORATE SOURCE: NATL INST PUBL HLTH & ENVIRONM PROTECT,POB 1/3720 BA BILTHOVEN//NETHERLANDS/ (Reprint); UNIV HOSP LEIDEN,DEPT IMMUNOHAEMATOL & BLOODBANK/2300 RC LEIDEN//NETHERLANDS/
PUBLICATION: JOURNAL OF IMMUNOLOGY, 1991, V147, N6 (SEP 15), P2012-2018
GENUINE ARTICLE#: GG108
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: No vaccine is yet available against serogroup B meningococci, which are a common cause of bacterial meningitis. Some outer membrane proteins (OMP), **LPS**, and capsular polysaccharides have been identified as protective Ag. The amino acid sequence of the protective B cell epitopes present within the class 1 OMP has been described recently. Synthetic peptides containing OMP B cell epitopes as well as capsular polysaccharides or **LPS** protective B cell epitopes have to be presented to the immune system in association with T cell epitopes to achieve an optimal Ir. The use of homologous, i.e., meningococcal, T cell epitopes has many advantages. We therefore investigated recognition sites for human T cells within the meningococcal class 1 OMP. We have synthesized 16 class 1 OMP-derived peptides encompassing predicted T cell epitopes. Peptides corresponding to both surface loops and trans-membrane regions (some of which occur as amphipathic beta-sheets) of the class 1 OMP were found to be recognized by T cells. In addition, 10 of 11 peptides containing predicted amphipathic alpha-helices and four of five peptides containing T cell epitope motifs according to Rothbard and Taylor (Rothbard, J. B., and W. R. Taylor. 1988. EMBO J 7:93) were recognized by lymphocytes from one or more volunteers. Some of the T and B cell epitopes were shown to map to identical regions of the protein. At least six of the peptides that were found to contain T cell epitopes show homology to constant regions of the meningococcal class 3 OMP and the **gonococcal** porins PIA and PIB. Peptide-specific T cell lines and T cell clones were established to investigate peptide recognition in more detail. The use of a panel of HLA-typed APC revealed clear HLA-DR restriction patterns. It seems possible now to develop a (semi-) synthetic meningococcal vaccine with a limited number of constant T cell epitopes that cover all HLA-DR locus products.

10/3,AB/16 (Item 15 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02786794 References: 62
TITLE: ENDOGENOUS SIALYLATION OF THE **LIPOOLIGOSACCHARIDES** OF NEISSERIA-MENINGITIDIS
AUTHOR(S): MANDRELL RE; KIM JJ; JOHN CM; GIBSON BW; SUGAI JV; APICELLA MA; GRIFFISS JM; YAMASAKI R
CORPORATE SOURCE: VET ADM MED CTR,CTR IMMUNOCHEM,4150 CLEMENT ST/SAN FRANCISCO//CA/94121 (Reprint); UNIV CALIF SAN FRANCISCO,DEPT LAB MED/SAN FRANCISCO//CA/94143; UNIV CALIF SAN FRANCISCO,DEPT PHARMACEUT CHEM/SAN FRANCISCO//CA/94143; SUNY BUFFALO,DEPT MED/BUFFALO//NY/14215
PUBLICATION: JOURNAL OF BACTERIOLOGY, 1991, V173, N9 (MAY), P2823-2832
GENUINE ARTICLE#: FK038
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Monoclonal **antibodies** (MAb) 3F11 and 06B4 recognize epitopes that are conserved on **gonococcal lipooligosaccharides** (**LOS**), present on some **meningococcal LOS**, and conserved on human erythrocytes. **LOS** of some **group B** and C prototype **meningococcal LOS** strains (**LOS** serotypes L1 to L8) treated with neuraminidase showed increased expression of the 3F11 and 06B4 MAb-defined epitopes. Neuraminidase-treated **LOS** separated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and silver stained showed a shift in migration from a component with a mass of approximately 4.8 kDa to a component with a mass of between 4.5 and 4.6 kDa. The same strains grown in medium with excess CMP-N-acetylneuraminic acid had **LOS** that shifted in migration to a slightly higher component (mass, approximately 4.8 kDa). Chemical analysis of the neuraminidase-digested products from one **LOS** indicated it contained approximately 1.5% sialic acid. Covalent linkage between sialic acid and the **LOS** was confirmed by analysis of de-O-acylated and dephosphorylated **LOS** by liquid secondary ion mass spectrometry. These studies show that some meningococci contain sialic acid in their **LOS**, that the sialic acid is cleaved and lost in conventional acetic acid hydrolysis, and that the sialic acid alters the expression of MAb-defined epitopes.

10/3,AB/17 (Item 16 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

02741543 References: 27
TITLE: ANTIGENIC SIMILARITIES IN **LIPOPOLYSACCHARIDES** OF HAEMOPHILUS AND NEISSERIA AND EXPRESSION OF A DIGALACTOSIDE STRUCTURE ALSO PRESENT ON HUMAN CELLS
AUTHOR(S): VIRJI M; WEISER JN; LINDBERG AA; MOXON ER
CORPORATE SOURCE: UNIV OXFORD,JOHN RADCLIFFE HOSP,DEPT PEDIAT/OXFORD OX3 9DU//ENGLAND/ (Reprint); ROCKEFELLER UNIV,DEPT BACTERIOL & IMMUNOL/NEW YORK//NY/10021; KAROLINSKA INST,HUDDINGE UNIV HOSP,DEPT CLIN BACTERIOL/S-14186 HUDDINGE//SWEDEN/
PUBLICATION: MICROBIAL PATHOGENESIS, 1990, V9, N6 (DEC), P441-450

GENUINE ARTICLE#: FG238
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

10/3,AB/18 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01688625
Adjuvant for transcutaneous immunization
Adjuvant fur transkutane Immunisation
Adjuvant pour immunisation transcutanee
PATENT ASSIGNEE:
The Government of the United States of America, as represented by The Secretary of the Army, (991614), HQ USAMRMC, Fort Detrick, Frederick, MD 21701-5012, (US), (Applicant designated States: all)
INVENTOR:
Glenn, Gregory, 20 Firstfield Road, Suite 250, Giatherburg,MD 20878, (US)
Alving, Carl, 3 Newbolt Court, Bethesda, MD 20817, (US)
LEGAL REPRESENTATIVE:
Lipscombe, Martin John et al (80581), Keith W Nash & Co, Pearl Assurance House, 90-92 Regent Street, Cambridge CB2 1DP, (GB)
PATENT (CC, No, Kind, Date): EP 1384403 A1 040128 (Basic)
APPLICATION (CC, No, Date): EP 2003017154 971114;
PRIORITY (CC, No, Date): US 749164 961114; US 896085 970717
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 1014787 (EP 97947608)
INTERNATIONAL PATENT CLASS: A01N-037/18; A61F-013/00; A61K-039/00; A61K-009/127; A61K-009/52; A61K-009/56

ABSTRACT EP 1384403 A1
A transcutaneous immunization system delivers antigen to immune cells without perforation of the skin, and induces an immune response in an animal or human. The system uses an adjuvant, preferably an ADP-ribosylating exotoxin, to induce an antigen-specific immune response (e.g. humoral and/or cellular effectors) after transcutaneous application of a formulation containing antigen and adjuvant to intact skin of the animal or human. The efficiency of immunization may be enhanced by adding hydrating agents (e.g. liposomes), penetration enhancers, or occlusive dressings to the transcutaneous delivery system. This system may allow activation of Langerhans cells in the skin, migration of the Langerhans cells to lymph nodes, and antigen presentation.
ABSTRACT WORD COUNT: 108
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200405	611
SPEC A	(English)	200405	18489
Total word count - document A			19100
Total word count - document B			0
Total word count - documents A + B			19100

10/3,AB/19 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01673042
Medicament for the treatment of diseases due to infection by Neisseria Meningitidis
Arzneimittel zur Behandlung von infektiosen Krankheiten infolge Neisseria Meningitidis
Medicament pour le traitement des maladies causees par une infection de neisseria meningitidis
PATENT ASSIGNEE:
Braun, Jan Matthias, Dr., (4145490), Scheidtweilerstrasse 89, 50933 Koln, (DE), (Applicant designated States: all)
INVENTOR:
The designation of the inventor has not yet been filed
LEGAL REPRESENTATIVE:
Meyers, Hans-Wilhelm, Dr.Dipl.-Chem. et al (72541), Patentanwalte von Kreisler-Selting-Werner Postfach 10 22 41, 50462 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 1374892 A1 040102 (Basic)
APPLICATION (CC, No, Date): EP 2002014397 020628;
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/095; A61P-031/04

ABSTRACT EP 1374892 A1
The subject of the invention is a medicament for the treatment of diseases due to infection by Neisseria meningitidis, which comprises glycoconjugates and/or **lipooligosaccharides** (**LOS**) from commensal bacteria with cross-reactive antigens to Neisseria meningitidis and/or **antibodies** against such glycoconjugates and/or **lipooligosaccharides**.
ABSTRACT WORD COUNT: 42
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200401	390
SPEC A	(English)	200401	7642
Total word count - document A			8032
Total word count - document B			0
Total word count - documents A + B			8032

10/3,AB/20 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01624230
Antigenic iron repressible proteins from n. meningitidis related to the heolysin family of toxins

Mit der Familie der Hamolysin-Toxine verwandte Antigene Eisen-unterdruckende Proteine der N. Meningitis
Proteines antigeniques a action limitee par l'incorporation de fer tirees de la bacterie N. Meningitis et associees a la famille de toxines des hemolysines.
PATENT ASSIGNEE:
UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL, (751080), , Chapel Hill, North Carolina 27514, (US), (Applicant designated States: all)
INVENTOR:
Sparling, Frederick P., Route 1, Box 980, Moncure, NC 27559, (US)
Thompson, Stuart Alan, E6 Old Well Apartment, Carrboro, NC 27510, (US)
LEGAL REPRESENTATIVE:
Grunecker, Kinkeldey, Stockmair & Schwanhausser Anwaltssozietat (100721) , Maximilianstrasse 58, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1338607 A2 030827 (Basic)
APPLICATION (CC, No, Date): EP 2003004818 910716;
PRIORITY (CC, No, Date): US 552649 900716
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 539492 (EP 91913698)
INTERNATIONAL PATENT CLASS: C07K-014/22; C12N-015/31; C12N-015/11; A61K-038/16; A61K-039/095; C12Q-001/00; C07K-016/12

ABSTRACT EP 1338607 A2
The present invention is directed to antigenic polypeptides isolated from Neisseria meningitidis, **antibodies** raised against the polypeptides, vaccines containing the polypeptides and DNA encoding the polypeptides.
ABSTRACT WORD COUNT: 27
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200335	563
SPEC A	(English)	200335	7743
Total word count - document A			8306
Total word count - document B			0
Total word count - documents A + B			8306

10/3,AB/21 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01318947
Devices and methods for detection of an analyte based upon light interference
Vorrichtungen und Verfahren zur Detektion eines Analyten mittels optischer Interferenz
Dispositifs et methodes de detection d'un analyte bases sur l'interference de lumiere
PATENT ASSIGNEE:
BIOSTAR, INC., (1714370), 6655 Lookout Road, Boulder, CO 80301, (US), (Applicant designated States: all)

INVENTOR:
Bogart, Gregory R., 708 Riverside Avenue, Raritan, New Jersey 08869, (US)
Maul, Diana M., 1971 West 101st Court, Thornton, CO 80221, (US)
Crosby, Mark, 6655 Lookout Road, Boulder, CO 80301, (US)
Moddel, Garret R., 450 Marine Street, Boulder, CO 80302, (US)
Etter, Jeffrey B., 1318 Deer Trail Road, Boulder, CO 80302, (US)
Miller, John B., 7223 Four Rivers Road, Boulder, CO 80301, (US)
Blessing, James, 5144 Buckingham Road, Boulder, CO 80301, (US)
Kelley, Howard, 7181 Four Rivers Road, Boulder, CO 80301, (US)
Sandstrom, Torbjorn, Banvagen 56, 435 43 Molnylcke, (SE)
Stiblert, Lars, Delsjovagen 51, 412 70 Gotebor, (SE)
LEGAL REPRESENTATIVE:
Viering, Jentschura & Partner (100646), Steinsdorfstrasse 6, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1126278 A2 010822 (Basic)
EP 1126278 A3 011017
APPLICATION (CC, No, Date): EP 2001108521 930610;
PRIORITY (CC, No, Date): US 924343 920731
DESIGNATED STATES: DE; ES; FR; GB; IT
RELATED PARENT NUMBER(S) - PN (AN):
EP 727038 (EP 93915341)
INTERNATIONAL PATENT CLASS: G01N-035/00; G01N-033/543; G01N-033/52; B01L-003/00

ABSTRACT EP 1126278 A2
The invention refers to an optical assay device comprising:
- an active receptive surface supported on a pedestal and held within a first container; said first container comprising first absorbent material located at the base of said pedestal, configured and arranged to absorb liquid draining from said surface,
- a second container, hingedly connected to one side of said first container, said second container comprising a second absorbent material, wherein said second container can be closed to said first container by rotation about the hinge, and wherein such closing causes said second absorbent material to contact said surface.
ABSTRACT WORD COUNT: 99
NOTE:
Figure number on first page: 8B

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200134	624
SPEC A	(English)	200134	41381
Total word count - document A			42005
Total word count - document B			0
Total word count - documents A + B			42005

10/3,AB/22 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01261676
Method for differentiating microorganisms in a sample
Verfahren zur Unterscheidung von Mikroorganismen in eine Probe

Methode pour la differentiation des microorganismes dans un echantillon
PATENT ASSIGNEE:
Becton, Dickinson and Company, (2594831), 1 Becton Drive, Franklin Lakes, New Jersey 07417, (US), (Applicant designated States: all)
INVENTOR:
Gosnell, C. Michael, 1208 Mill Creek Road, Fallston, Maryland 21047, (US)
Hughes, Carrie A., 3 Briar Grove Court, Parkton, Maryland 21120, (US)
Goldenbaum, Paul E., 3931 Brittany Lane, Hampstead, Marylane 21074, (US)
LEGAL REPRESENTATIVE:
von Kreisler, Alek, Dipl.-Chem. et al (12437), Patentanwalte, von Kreisler-Selting-Werner, Bahnhofsvorplatz 1 (Deichmannhaus), 50667 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 1088897 A2 010404 (Basic)
EP 1088897 A8 010606
EP 1088897 A3 040102
APPLICATION (CC, No, Date): EP 2000116946 000807;
PRIORITY (CC, No, Date): US 407638 990928
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12Q-001/04

ABSTRACT EP 1088897 A2 (Translated)
Differentiation of microorganisms by color change on a blood- or hemin-containing nutrient medium containing a chromogen
Differentiating microorganisms in a sample comprises growing the microorganisms on a chromogenic indicator medium comprising a blood- or hemin-containing nutrient medium and a chromogen and detecting a color change among the microorganisms.
Independent claims are also included for the following:
(1) preparing chromogenic media containing blood or hemin, comprising applying a chromogenic substrate to a surface of a previously prepared nutrient medium, where the chromogenic substrate is carried in a solvent; and
(2) preparing chromogenic media containing blood or hemin, comprising adding a chromogenic substrate to a culture medium when the medium is prepared and before distribution to plates or tubes.
TRANSLATED ABSTRACT WORD COUNT: 117

ABSTRACT EP 1088897 A2
Culture media for microorganisms containing blood or hemin, particularly Trypticase Soy Agar with blood, and chocolate agar, are combined with known chromogenic substrates to produce chromogenic media. Methods for preparing these chromogenic media include adding chromogenic substrates to the surface of previously prepared media, or incorporating the chromogenic substrate into the media as it is prepared. Methods for distinguishing microorganisms in a sample using these culture media are also described.
ABSTRACT WORD COUNT: 71

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200114	313
SPEC A	(English)	200114	3871
Total word count - document A			4184

Total word count - document B 0
Total word count - documents A + B 4184

10/3,AB/23 (Item 6 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01261675
Chromogenic media containing blood or hemin
Blut oder Hamin enthaltende farbige Medien
Milieux chromogenes contenant le sang ou l'hemine
PATENT ASSIGNEE:
Becton, Dickinson and Company, (2594831), 1 Becton Drive, Franklin Lakes, New Jersey 07417, (US), (Applicant designated States: all)
INVENTOR:
Gosnell, C. Michael, 1208 Mill Creek Road, Fallston, Maryland 21047, (US)
Hughes, Carrie A., 3 Briar Grove Court, Parkton, Maryland 21120, (US)
Goldenbaum, Paul E., 3931 Brittany Lane, Hamstead, Maryland 21074, (US)
LEGAL REPRESENTATIVE:
von Kreisler, Alek, Dipl.-Chem. et al (12437), Patentanwalte, von Kreisler-Selting-Werner, Bahnhofsvorplatz 1 (Deichmannhaus), 50667 Koln, (DE)
PATENT (CC, No, Kind, Date): EP 1088896 A2 010404 (Basic)
EP 1088896 A3 040102
APPLICATION (CC, No, Date): EP 2000116945 000807;
PRIORITY (CC, No, Date): US 407637 990928
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12Q-001/04

ABSTRACT EP 1088896 A2
Culture media for microorganisms containing blood or hemin, particularly Trypticase Soy Agar with blood, and chocolate agar, are combined with known chromogenic substrates to produce chromogenic media. Methods for preparing these chromogenic media include adding chromogenic substrates to the surface of previously prepared media, or incorporating the chromogenic substrate into the media as it is prepared. Methods for distinguishing microorganisms in a sample using these culture media are also described.
ABSTRACT WORD COUNT: 71

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200114	128
SPEC A	(English)	200114	3860

Total word count - document A 3988
Total word count - document B 0
Total word count - documents A + B 3988

10/3,AB/24 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01184735
Transnasal transport/immunisation with highly adaptable carriers
Transnasaler Transport bzw. Impfung mit hochadaptierbaren Tragern
Transport/immunisation transnasale avec vehicules tres adaptables
PATENT ASSIGNEE:
IDEA AG, (2644731), Frankfurter Ring 193a, 80807 Munich, (DE),
(Proprietor designated states: all)
INVENTOR:
Stieber, Juliane, Clemensstr. 74, 80769 Munchen, (DE)
Chopra, Amia, A/21A, Ashok Vihar, Ohase 1, Delhi, 110052, (IN)
Cevc, Gregor, Erich-Kastner-Weg 16, 85551 Kirchheim, (DE)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1031347 A1 000830 (Basic)
EP 1031347 B1 020417
APPLICATION (CC, No, Date): EP 99101480 990127;
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; RO; SI
INTERNATIONAL PATENT CLASS: A61K-009/127; A61K-038/19; A61K-039/39; A61K-038/28

ABSTRACT EP 1031347 A1
The invention deals with the transport of preferably large molecules across nasal mucosa by means of specially designed, highly adaptable carriers loaded with said molecules. One of the purposes of making such formulations is to achieve non-invasive systemic delivery of therapeutic polypeptides, proteins and other macromolecules; the other intent is to overcome circumstantially the blood-brain barrier by exploiting the nasal cavity to enter the body and then to get access to the brain. A third intent is to achieve successful protective or tolerogenic immunisation via nasal antigen or allergen administration.
ABSTRACT WORD COUNT: 91
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200035	3796
CLAIMS B	(English)	200216	2702
CLAIMS B	(German)	200216	2544
CLAIMS B	(French)	200216	3251
SPEC A	(English)	200035	18066
SPEC B	(English)	200216	17452
Total word count - document A			21867
Total word count - document B			25949
Total word count - documents A + B			47816

10/3,AB/25 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01184734

Noninvasive vaccination through the skin
Nichtinvasive Impfung durch die Haut
Vaccination non invasive a travers la peau
PATENT ASSIGNEE:
IDEA AG, (2644731), Frankfurter Ring 193a, 80807 Munich, (DE),
(Proprietor designated states: all)
INVENTOR:
Chopra, Amia, A/21A, Ashok Vihar, Ohase 1, Delhi, 110052, (IN)
Cevc, Gregor, Erich-Kastner-Weg 16, 85551 Kirchheim, (DE)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100314), Siebertstrasse 4, 81675 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1031346 A1 000830 (Basic)
EP 1031346 B1 020502
APPLICATION (CC, No, Date): EP 99101479 990127;
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV; RO; SI
INTERNATIONAL PATENT CLASS: A61K-009/127; A61K-038/19; A61K-039/39

ABSTRACT EP 1031346 A1
The present invention relates to novel vaccines for the non-invasive, transcutaneous administration of antigens associated with ultradeformable carriers, for the purpose of prophylactic or therapeutic vaccination. The vaccines comprise (a) a transdermal carrier; (b) a compound which specifically releases or specifically induces cytokine or anti-cytokine activity or exerts such an activity itself, and (c) an antigen or an allergen. The invention further relates to methods for the vaccination of mammals for obtaining a protective or therapeutic immune response.
ABSTRACT WORD COUNT: 79
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200035	2035
CLAIMS B	(English)	200218	2055
CLAIMS B	(German)	200218	1886
CLAIMS B	(French)	200218	2133
SPEC A	(English)	200035	14673
SPEC B	(English)	200218	14771
Total word count - document A			16711
Total word count - document B			20845
Total word count - documents A + B			37556

10/3,AB/26 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01070801
Antigenic conjugates of conserved **lipopolysaccharides** of gram negative bacteria
Antigenkonjugate von konservierten **Lipopolysacchariden** aus gram-negativen Bakterien
Conjugues antigeniques de **lipopolysaccharides** de bacteries

gram-negatives
PATENT ASSIGNEE:
American Cyanamid Company, (212598), Five Giralda Farms, Madison, New Jersey 07940-0874, (US), (Applicant designated States: all)
INVENTOR:
Arumugham, Rasappa G., 15 Elatia Circle Pittsford, New York 14534, (US)
Fortuna-Nevin, Maria, 696 Summit Drive, Webster, New York 14580, (US)
Apicella, Michael A., 2626 Johnson Crossing, Solon, Iowa 52333, (US)
Gibson, Bradford W., 1324 Peralta Avenue, Berkeley, California 94702, (US)
LEGAL REPRESENTATIVE:
Wileman, David Francis, Dr. et al (46002), c/o Wyeth Laboratories Huntercombe Lane South, Taplow Maidenhead Berkshire SL6 OPH, (GB)
PATENT (CC, No, Kind, Date): EP 941738 A1 990915 (Basic)
APPLICATION (CC, No, Date): EP 99301747 990309;
PRIORITY (CC, No, Date): US 37529 980310
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/385; A61K-039/02; A61K-39:095

ABSTRACT EP 941738 A1
Antigenic conjugates are provided which comprise a carrier protein covalently bonded to the conserved portion of a **lipopolysaccharide** of a gram negative bacteria, wherein said conserved portion of the **lipopolysaccharide** comprises the inner core and lipid A portions of said **lipopolysaccharide**, said conjugate eliciting a cross reactive immune response against heterologous strains of said gram negative bacteria.
ABSTRACT WORD COUNT: 58
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9937	707
SPEC A	(English)	9937	6253
Total word count - document A			6960
Total word count - document B			0
Total word count - documents A + B			6960

10/3,AB/27 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00937202
MONOCLONAL **ANTIBODIES** THAT DEFINE UNIQUE MENINGOCOCCAL B EPITOPES AND THEIR USE IN THE PREPARATION OF VACCINE COMPOSITIONS
MENINGOKOKKUS B-EPITOP AUSBILDENDE MONOKLONALE ANTIKOERPER UND DEREN VERWENDUNG ZUR HERSTELLUNG VON IMPFSTOFFZUSAMMENSTELLUNGEN
ANTICORPS MONOCLONAUX DEFINISSANT DES EPITOPES MENINGOCOCCIQUES B ET LEURS UTILISATIONS DANS LA PREPARATION DE COMPOSITIONS VACCINALES
PATENT ASSIGNEE:
CHIRON CORPORATION, (572530), 4560 Horton Street, Emeryville, California

94608, (US), (Proprietor designated states: all)
CHILDREN'S HOSPITAL MEDICAL CENTER OF NORTHERN CALIFORNIA, (389081), 747 Fifty Second Street, Oakland, CA 94609, (US), (Proprietor designated states: all)
INVENTOR:
GRANOFF, Dan, 1085 Creston Road, Berkeley, CA 94708, (US)
MOE, Gregory, R., 42 Steuben Bay, Alameda, CA 94502, (US)
LEGAL REPRESENTATIVE:
Hallybone, Huw George et al (53031), Carpmaels and Ransford, 43 Bloomsbury Square, London WC1A 2RA, (GB)
PATENT (CC, No, Kind, Date): EP 922059 A1 990616 (Basic)
EP 922059 B1 031022
WO 98008874 980305
APPLICATION (CC, No, Date): EP 97941371 970827; WO 97US15167 970827
PRIORITY (CC, No, Date): US 25799 960827
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C07K-016/12; A61K-039/095; C12N-005/12; G01N-033/50; C07K-016/42; C07K-007/06; A61K-038/08
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200343	317
CLAIMS B	(German)	200343	300
CLAIMS B	(French)	200343	380
SPEC B	(English)	200343	19435
Total word count - document A			0
Total word count - document B			20432
Total word count - documents A + B			20432

10/3,AB/28 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00862554
THERAPEUTIC AND DIAGNOSTIC AGENTS FOR THE TREATMENT OF MICROBIAL INFECTIONS
THERAPEUTISCHE UND DIAGNOSTISCHE AGENZIEN ZUR BEHANDLUNG MIKROBIELLER INFEKTIONEN
AGENTS THERAPEUTIQUES ET DE DIAGNOSTIC POUR TRAITER LES INFECTIONS MICROBIENNES
PATENT ASSIGNEE:
Montana State University, (4352824), 304 Montana Hall, Bozeman, MT 59717, (US), (Proprietor designated states: all)
Ligocyte Pharmaceuticals, Inc., (2984800), 920 Technology Blvd., Suite C., Bozeman, MT 59718, (US), (Proprietor designated states: all)
INVENTOR:
PASCUAL, David, 8220 Indian Paint Brush Drive, Bozeman, MT 59178, (US)
BURRITT, James, 1215 S. Bozeman, Bozeman, MT 59715, (US)
BURGESS, Don, 5553 Black Bear, Bozeman, MT 59715, (US)
GLEE, Pati, 813 W. Villard 75, Bozeman, MT 59718, (US)
JUTILA, John, 516 S. Grand Avenue, Bozeman, MT 59715, (US)
JUTILA, Mark, 3308 Sundance Drive, Bozeman, MT 59715, (US)
BARGATZE, Robert, 1302 Wildflower Way, Bozeman, MT 59715, (US)

PYLE, Barry, 4985 Foster Lane, Bozeman, MT 59175, (US)
CUTLER, Jim, E., 1426 Ash Drive, Bozeman, MT 59715, (US)
HAN, Yongmoon, 306 Treasure Avenue, Bozeman, MT 59715, (US)
LEGAL REPRESENTATIVE:
Gervasi, Gemma, Dr. et al (40515), Notarbartolo & Gervasi S.p.A., Corso di Porta Vittoria, 9, 20122 Milano, (IT)
PATENT (CC, No, Kind, Date): EP 869801 A2 981014 (Basic)
EP 869801 B1 040121
WO 1997018790 970529
APPLICATION (CC, No, Date): EP 96942049 961121; WO 96US18796 961121
PRIORITY (CC, No, Date): US 7477 P 951122
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-035/12
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200404	1868
CLAIMS B	(German)	200404	1706
CLAIMS B	(French)	200404	2300
SPEC B	(English)	200404	20527
Total word count - document A			0
Total word count - document B			26401
Total word count - documents A + B			26401

10/3,AB/29 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00656876
GONOCOCCAL ANTI-IDIOTYPIC **ANTIBODIES** AND METHODS AND COMPOSITIONS USING THEM
Anti idiotypische Antikorper gegen **Gonococcen** und diese verwendende Verfahren und Zusammensetzungen.
ANTICORPS ANTI-IDIOTYPIQUES **GONOCOCCIQUES** ET PROCEDES ET COMPOSITIONS LES UTILISANT
PATENT ASSIGNEE:
Rice, Peter A., (3024480), 55 Norfolk Road, Chestnut Hill, MA 02167, (US), (Proprietor designated states: all)
Gulati, Sunita, (3024490), 14 Wheeler Street, Gloucester, MA 01930, (US), (Proprietor designated states: all)
McQuillen, Daniel P., (3024500), 9 Holland Terrace, Needham, MA 02192, (US), (Proprietor designated states: all)
INVENTOR:
Rice, Peter A., 55 Norfolk Road, Chestnut Hill, MA 02167, (US)
Gulati, Sunita, 14 Wheeler Street, Gloucester, MA 01930, (US)
McQuillen, Daniel P., 9 Holland Terrace, Needham, MA 02192, (US)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, 81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 695192 A1 960207 (Basic)
EP 695192 B1 010228
WO 9422479 941013
APPLICATION (CC, No, Date): EP 94912962 940406; WO 94US3794 940406

PRIORITY (CC, No, Date): US 43663 930406
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: A61K-039/395; C12P-021/08; C12N-005/12; G01N-033/569
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200109	497
CLAIMS B	(German)	200109	479
CLAIMS B	(French)	200109	494
SPEC B	(English)	200109	16656
Total word count - document A			0
Total word count - document B			18126
Total word count - documents A + B			18126

10/3,AB/30 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00646348
Preparation and uses of **LOS** -depleted outer membrane proteins of gram-negative cocci
Herstellung und Verwendungen von **LOS** -verminderten Aussenmembran-Proteinen von Gram-negativen Kokken
Preparation et utilisations de proteines de membranes externes depouvues de **LOS** a partir de coques gram-negatifs
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212592), One Cyanamid Plaza, Wayne New Jersey 07470, (US), (Proprietor designated states: all)
INVENTOR:
Zlotnick, Gary W., 21 Woodlyn Way, Penfield, New York 14526, (US)
LEGAL REPRESENTATIVE:
Wachtershauser, Gunter, Prof. Dr. (12711), Patentanwalt, Tal 29, 80331 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 624376 A1 941117 (Basic)
EP 624376 B1 000315
APPLICATION (CC, No, Date): EP 94106827 940502;
PRIORITY (CC, No, Date): US 61581 930513
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; NL; PT; SE
EXTENDED DESIGNATED STATES: SI
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/40

ABSTRACT EP 624376 A1
Described herein is a method for removing toxic **lipooligosaccharide** (**LOS**) from outer membranes of Gram-negative cocci, such as Neisseria meningitidis. **LOS**-depleted outer membranes and **LOS**-depleted soluble outer membrane proteins can be prepared, which are able to elicit bactericidal **antibodies** against homologous strains of bacteria. Vaccines and other uses of the preparations are further described.
ABSTRACT WORD COUNT: 56

NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200011	865
CLAIMS B	(German)	200011	798
CLAIMS B	(French)	200011	1006
SPEC B	(English)	200011	5445
Total word count - document A			0
Total word count - document B			8114
Total word count - documents A + B			8114

10/3,AB/31 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00506998
ANTIGENIC IRON REPRESSIBLE PROTEINS FROM N. MENINGITIDIS RELATED TO THE HEMOLYSIN FAMILY OF TOXINS
MIT DER FAMILIE DER HAMOLYSIN-TOXINE VERWANDTE ANTIGENE EISEN-UBNTERDRUCKENDE PROTEINE DES N. MENINGITIS
PROTEINES ANTIGENIQUES A ACTION LIMITEE PAR L'INCORPORATION DE FER TIREES DE LA BACTERIE N. MENINGITIDIS ET ASSOCIEES A LA FAMILLE DE TOXINES DES HEMOLYSINES
PATENT ASSIGNEE:
UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL, (751080), , Chapel Hill, North Carolina 27514, (US), (Proprietor designated states: all)
INVENTOR:
SPARLING, P., Frederick, Route 1, Box 980, Moncure, NC 27559, (US)
THOMPSON, Stuart, Alan, E6 Old Well Apartment, Carrboro, NC 27510, (US)
LEGAL REPRESENTATIVE:
Grunecker, Kinkeldey, Stockmair & Schwanhausser Anwaltssozietat (100721) , Maximilianstrasse 58, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 539492 A1 930505 (Basic)
EP 539492 A1 930901
EP 539492 B1 030611
WO 92001460 920206
APPLICATION (CC, No, Date): EP 91913698 910716; WO 91US5014 910716
PRIORITY (CC, No, Date): US 552649 900716
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
RELATED DIVISIONAL NUMBER(S) - PN (AN):
(EP 2003004818)
INTERNATIONAL PATENT CLASS: C07K-014/22; C12N-015/31; C12N-015/11; A61K-038/16; A61K-039/095; C12Q-001/00; C07K-016/12
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200324	2234
CLAIMS B	(German)	200324	2069
CLAIMS B	(French)	200324	2358
SPEC B	(English)	200324	9791

Total word count - document A 0
Total word count - document B 16452
Total word count - documents A + B 16452

10/3,AB/32 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00506711
IMPROVED ADJUVANTS AND VACCINES
VERBESSERTE ADJUVANTIEN UND IMPFSTOFFE
ADJUVANTS ET VACCINS AMELIORES
PATENT ASSIGNEE:
EMORY UNIVERSITY, (382080), 1380 South Oxford Road, Atlanta, GA 30322, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
HUNTER, Robert, L., 3640 Churchwell Street, Tucker, GA 30084, (US)
TAKAYAMA, Kuni, K., 6517 Inner Drive, Madison, WI 53705, (US)
LEGAL REPRESENTATIVE:
Fleischer, Holm Herbert, Dr. et al (79601), Patentanwalte Dr. H.-G. Sternagel, Dr. H. Fleischer, Dr. H. Dorries, Sander Aue 30, 51465 Bergisch Gladbach, (DE)
PATENT (CC, No, Kind, Date): EP 536302 A1 930414 (Basic)
EP 536302 A1 930804
EP 536302 B1 970827
WO 9200101 920109
APPLICATION (CC, No, Date): EP 91913213 910627; WO 91US4716 910627
PRIORITY (CC, No, Date): US 544831 900627; US 716807 910621
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/42; A61K-039/40; A61K-039/00; A61K-039/02; C07K-014/00;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	9708W4	222
CLAIMS B	(German)	9708W4	201
CLAIMS B	(French)	9708W4	223
SPEC B	(English)	9708W4	8476

Total word count - document A 0
Total word count - document B 9122
Total word count - documents A + B 9122

10/3,AB/33 (Item 16 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00478178
Nucleotide sequence coding for an outer membrane protein from Neisseria meningitidis and use of said protein in vaccine preparations
Nukleotidsequenz, die fur ein Aussenmembran-Protein von Neisseria meningitidis kodiert und Verwendung dieses Proteins zur Herstellung von

Impfstoffen
Sequence nucleotidique codant pour une proteine de la membrane externe de Neisseria meningitidis, et utilisation de cette proteine dans la preparation de vaccin

PATENT ASSIGNEE:
CENTRO DE INGENIERIA GENETICA Y BIOTECNOLOGIA, (1256830), 31 Street, '/156 & 190, Cubanacan Playa, Havana, (CU), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Rodriguez, Ricardo Silva, Calle 15 No. 4209, entre 42 y 44, Playa, La Habana, (CU)
Houssein Sosa, Manuel Selman, Paseo No. 126, entre 5ta y Calzada, Vedado, La Habana, (CU)
Nieto, Gerardo Guillen, Linea No.6, Apto 4, entre N y O, Vedado, La Habana, (CU)
Herrera Martinez, Luis S. Centro Ingenieria, Genetica y Biotecnoligia 31 Str., '/156 & 190, Cubanacan. Playa Havana, (CU)
Fernandez Maso, Julio RaUl, Calle 26 No.873 1-2,Apto 3, entre Conill y45,Nuevo, La Habana, (CU)
Novoa Perez, Lidia Ines, Calle 184 No.3112, entre 31 y 33, Apto 49, Playa , La Habana, (CU)
Grillo, Juan Morales, Compostela No.653, Apto 1, entre Luz y Acosta, Habana Vieja, La Habana, (CU)
Morera Cordova, Vivian, Calle 184 No.3112, entre 31 y 33, Apto 39, Playa, La Habana, (CU)
Gonzalez Blanco, Sonia, Calle 184 No.3112, entre 31 y 33, Apto 42, Playa, La Habana, (CU)
Santos, Beatriz Tamargo, Calle 202 No.29302, entre 293y295, Reparto Calixto, Sanchez, Boyeros, La Habana, (CU)
del Valle Rosales, JesUs Augusto, D'Strampes N.351, entre San Mariano y Vista Alegre, La Vibora, La Habana, (CU)
Menendez, Evelin Caballero, Calle 7 No.214, entre 2 y 4, Cayo de la Rosa, Bauta, La Habana, (CU)
Alvarez Acosta, Anabel, Calle 184 No.3112, entre 31 y 33, Apto 1, Playa, La Habana, (CU)
Couzeau Rodriguez, Edelgis, Calle 184 No.3112, entre 31 y 33, Apto 20, Playa, La Habana, (CU)
Cruz Leon, Silian, Ave 47 No.11812, entre 118 y 120, Marianao, La Habana, (CU)
Musacchio Lasa, Alexis, Calle 128 No.7117, entre 71 y 73, Mariel, La Habana, (CU)
LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 97, 2587 BN 's-Gravenhage, (NL)

PATENT (CC, No, Kind, Date): EP 474313 A2 920311 (Basic)
EP 474313 A3 930224
EP 474313 B1 970423
APPLICATION (CC, No, Date): EP 91202291 910906;
PRIORITY (CC, No, Date): CU 14590 900907
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; A61K-039/095; C12P-021/08; C12N-015/62; C12N-015/53; C12N-015/54; C12N-001/21; C12N-001/21; C12R-001/19

ABSTRACT EP 474313 A2
The present invention is concerned with a method for the isolation of a

nucleotide sequence which codes for a protein having a molecular weight of about 64 000 daltons, which is located on the outer membrane of N. meningitidis, as well as with the recombinant DNA obtained therefrom, which is used for the transformation of a host microorganism. The technical object pursued with the invention is the identification of a nucleotide sequence coding for a highly conserved and common protein for the majority of **pathogenic Neisseria** strains, the production of this protein with a high level of purity and in commercially useful amounts using the recombinant way, so that it can be used in diagnostic methods and vaccine preparations with a broad immunoprotection spectrum. (see image in original document)
ABSTRACT WORD COUNT: 131

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	765
CLAIMS B	(English)	EPAB97	305
CLAIMS B	(German)	EPAB97	313
CLAIMS B	(French)	EPAB97	323
SPEC A	(English)	EPABF1	6148
SPEC B	(English)	EPAB97	6260
Total word count - document A			6913
Total word count - document B			7201
Total word count - documents A + B			14114

10/3,AB/34 (Item 17 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00443912
MENINGOCOCCAL CLASS 1 OUTER-MEMBRANE PROTEIN VACCINE
MENINGOCOCCALES KLASSE I-AUSSENMEMBRANPROTEIN-VAKZIN
VACCIN MENINGOCOQUE DE LA PROTEINE DE LA MEMBRANE EXTERNE DE LA CLASSE 1
PATENT ASSIGNEE:
AMERICAN CYANAMID COMPANY, (212595), One Portland Square, Portland, Maine 04101, (US), (Proprietor designated states: all)
De Staat der Nederlanden, represented by the Deputy Director-General of the RIVM of Bilthoven, (935230), Antonie van Leeuwenhoeklaan 9, NL-3720 BA Bilthoven, (NL), (Proprietor designated states: all)
INVENTOR:
SEID, Robert, C., Jr., 590 25th Avenue, San Francisco, CA 94121, (US)
PARADISO, Peter, R., 6 Guilford Way, Pittsford, NY 14534, (US)
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HOOGERHOUT, Peter, Idenburgstraat 13, NL-2805 SZ Gouda, (NL)
WIERTZ, Emmanuel, J., H., J., Mauritsstraat 106, NL-3583 HW Utrecht, (NL)
VAN DER LEY, Peter, Adriaan van Ostadelaan 124, NL-3583 AM Utrecht, (NL)
HECKELS, John, Edward 6 Arun Way West Wellow, Romsey, Hampshire SO51 6GT, (GB)
CLARKE, Ian, Nicholas 15 Fernyhurst Avenue, Rownhams Southampton, Hampshire SO1 8DR, (GB)
LEGAL REPRESENTATIVE:
Roques, Sarah Elizabeth et al (79543), J.A. Kemp & Co. 14 South Square Gray's Inn, London WC1R 5JJ, (GB)
PATENT (CC, No, Kind, Date): EP 449958 A1 911009 (Basic)

EP 449958 B1 950322
EP 449958 B2 021113
EP 449958 B9 030528
WO 90006696 900628
APPLICATION (CC, No, Date): EP 90901397 891219; WO 89US5678 891219
PRIORITY (CC, No, Date): NL 883111 881219; NL 8936 890106; NL 891612 890626
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; C07K-014/22; C07K-007/04; A61K-039/39; A61K-039/385; C12N-015/31; C12N-015/62; C12N-15:31; C12R-1:36
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200322	2220
CLAIMS B	(German)	200322	2206
CLAIMS B	(French)	200322	2873
SPEC B	(English)	200322	14678
Total word count - document A			0
Total word count - document B			21977
Total word count - documents A + B			21977

10/3,AB/35 (Item 18 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00384471
T-CELL EPITOPE AS CARRIERS MOLECULE FOR CONJUGATE VACCINES.
T-ZELLEN-EPITOPE ALS TRAGER FUR EINEN KONJUGIERTEN IMPFSTOFF.
EPITOPES DE CELLULES T A TITRE DE MOLECULES PORTEUSES POUR VACCINS CONJUGUES.
PATENT ASSIGNEE:
PRAXIS BIOLOGICS, INC., (693521), 30 Corporate Woods, Rochester New York 14623, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
BIXLER, Garvin, 92 Squirrel's Heath Road, Fairport, NY 11450, (US)
PILLAI, Subramonia, 286 Vollmer Parkway, Rochester, NY 14623, (US)
INSEL, Richard, 167 Oakdale Drive, Rochester, NY 14618, (US)
LEGAL REPRESENTATIVE:
Allam, Peter Clerk et al (27601), LLOYD WISE, TREGEAR & CO. Norman House 105-109 Strand, London WC2R 0AE, (GB)
PATENT (CC, No, Kind, Date): EP 399001 A1 901128 (Basic)
EP 399001 B1 940727
WO 8906974 890810
APPLICATION (CC, No, Date): EP 89908669 890131; WO 89US388 890131
PRIORITY (CC, No, Date): US 150688 880201
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/385; C07K-015/04; A61K-039/155;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count

CLAIMS B	(English)	EPBBF1	747
CLAIMS B	(German)	EPBBF1	655
CLAIMS B	(French)	EPBBF1	800
SPEC B	(English)	EPBBF1	13397

Total word count - document A 0
Total word count - document B 15599
Total word count - documents A + B 15599

10/3,AB/36 (Item 19 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00324527
Vaccine against **group B Neisseria meningitidis**, gammaglobulin and transfer factor.
Vakzin gegen Neisseria meningitidis Gruppe-B, Gammaglobulin und Transferfaktor.
Vaccin contre Neisseria meningitidis groupe B, gammaglobuline et facteur de transfert.
PATENT ASSIGNEE:
CENTRO NACIONAL DE BIOPREPARADOS, (1010410), 1914, 212 Street Atabey, Playa, La Habana, (CU), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
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Sierra Gonzalez, Victoriano Gustavo, 101, San Pedro St. Santa Clara, Villa Clara, (CU)
Gutierrez Vazquez, Maria Mercedes, A Street No. 1302 Bejucal, La Habana, (CU)
Bisset Jorrin, Gonzalo, 563, San Miguel Street Barrio Obrero, La Habana, (CU)
Garcia Imia, Luis Guillermo, Mercado Street Barrio Obrero, La Habana, (CU)
Puentes Rizo, Gisela de la Caridad, Maria Luisa Street No. 682 Mantilla, La Habana, (CU)
Sampedro Herrera, Maria del Carmen, 615, Delicia Street, Lawton, La Habana, (CU)
Sotolongo Padron, Franklin, 72, Santo Suarez Street, La Habana, (CU)
Xochitl le Riverend Morales, Eloisa, 31, Loma Avenue Nuevo Vedado, La Habana, (CU)
Galguera Dominguez, Manuel Alfredo, 9, 9na. Street Santa Clara, Villa Clara, (CU)
LEGAL REPRESENTATIVE:
Gil-Vega, Victor (53451), Estebanez Calderon, 3 - 5B, E-28020 Madrid, (ES)
PATENT (CC, No, Kind, Date): EP 301992 A2 890201 (Basic)
EP 301992 A3 900214
EP 301992 B1 950524
APPLICATION (CC, No, Date): EP 88500077 880730;
PRIORITY (CC, No, Date): CU 12587 870730
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/095; A61K-039/40; C07K-002/00; A61K-035/14;

ABSTRACT EP 301992 A2

A method is provided for obtaining a vaccine against the different **pathogenic** serotypes of **group B Neisseria meningitidis** characterized by starting from live microorganisms of any one of the known pathogenic serotypes of the B group without inactivation, from which the extractation of the vesicles of the outer membrane and the protein antigenic complex of 65 - 95 KD molecular weight is carried out using detergent, enzyme and ultrasound combined in the treatment. The resulting product, after treatment to eliminate the nucleic acids, is purified by a dissociating treatment with detergent, ultrasonic bath and column chromatography. The multi-antigenic material so obtained is purified to obtain the protein antigenic complex of 65 - 95 KD molecular weight for HPLC chromatography (TSK 3000 SWG column) or affinity chromatography with monoclonal **antibodies**, or hydrophobicity chromatography, or ionic exchange chromatography or a combination of any one of them. The protein antigenic complex is then added to the fraction that contains the vesicles by ultrasound treatment so that it will be anchored on then, in a proportion of 15 por cent (+-) 3. The capsulr polysaccharide is also added, in a proportion of 1.1 - 1.4 with respect to the protein and the adjuvant in a relation ranging from 2 - 100 mcg/protein mcg. The different components ot the mixture may be sterilized by cobalt 60 inonizing radiations with doses from 5 - 25 Kgy and a temperature between 1 - 4 grade C before preparing the mixture or the resulting mixture may be sterilized by this procedure.
ABSTRACT WORD COUNT: 257

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	1009
CLAIMS B	(English)	EPAB95	969
CLAIMS B	(German)	EPAB95	919
CLAIMS B	(French)	EPAB95	1028
SPEC A	(English)	EPABF1	5555
SPEC B	(English)	EPAB95	5600
Total word count - document A			6564
Total word count - document B			8516
Total word count - documents A + B			15080

10/3,AB/37 (Item 20 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00282597
VACCINE AND METHOD OF PREPARATION.
IMPFSTOFF UND VERFAHREN ZUR HERSTELLUNG.
VACCIN ET PROCEDE DE PREPARATION.
PATENT ASSIGNEE:
EMORY UNIVERSITY, (382080), 1380 South Oxford Road, Atlanta, GA 30322, (US), (applicant designated states: AT;BE;CH;DE;FR;GB;IT;LI;LU;NL;SE)
INVENTOR:
HUNTER, Robert, L., 3640 Churchwell Court, Tucker, GA 30084, (US)
LEGAL REPRESENTATIVE:
Sternagel, Hans-Gunther, Dr. et al (46851), Patentanwalte Dr. Michael Hann Dr. H.-G. Sternagel Sander Aue 30, D-51465 Bergisch Gladbach, (DE)
PATENT (CC, No, Kind, Date): EP 283505 A1 880928 (Basic)

EP 283505 A1 891227
EP 283505 B1 940706
WO 8801873 880324
APPLICATION (CC, No, Date): EP 87906496 870819; WO 87US2056 870819
PRIORITY (CC, No, Date): US 909964 860922; US 75187 870716
DESIGNATED STATES: AT; BE; CH; DE; FR; GB; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/02; A61K-039/12; A61K-039/295; A61K-039/385;
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	824
CLAIMS B	(German)	EPBBF1	798
CLAIMS B	(French)	EPBBF1	849
SPEC B	(English)	EPBBF1	5734
Total word count - document A			0
Total word count - document B			8205
Total word count - documents A + B			8205

10/3,AB/38 (Item 21 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00268721
A method for culturing bordetella pertussis, a pertussis toxoid and a pertussis vaccine.
Verfahren zum Zuchten von Bordetella-Pertussis, ein Pertussis-Toxoid und ein Pertussis-Impfstoff.
Methode pour cultiver bordetella pertussis, un toxoide de pertussis et un vaccin contre pertussis.
PATENT ASSIGNEE:
The Research Foundation for Microbial Diseases of Osaka University, (884260), 3-1 Yamadaoka, Suita-shi Osaka, (JP), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Chazono, Masashi, 640-46 Muromoto-cho, Kanonzi-shi Kagawa-ken, (JP)
Yoshida, Iwao, 1247-2 Nagareoka-cho, Kanonzi-shi Kagawa-ken, (JP)
Konobe, Takeo, 9-24 Yahata-cho 1-chome, Kanonzi-shi Kagawa-ken, (JP)
Osame, Juichiro, 6784-191 Takuma Matoba Takuma-cho, Mitoyo-gun Kagawa-ken , (JP)
Takaku, Keisuke, 30-11 Senriyama-nishi 4-chome Senriyama, Suita-shi Osaka-fu, (JP)
LEGAL REPRESENTATIVE:
Lewin, John Harvey et al (33031), Elkington and Fife Prospect House 8 Pembroke Road, Sevenoaks, Kent TN13 1XR, (GB)
PATENT (CC, No, Kind, Date): EP 287732 A1 881026 (Basic)
EP 287732 B1 931020
APPLICATION (CC, No, Date): EP 87306165 870713;
PRIORITY (CC, No, Date): JP 86102360 870424
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/10; C12N-001/20; C12N-001/22;

ABSTRACT EP 287732 A1

There is disclosed a method for culturing Bordetella Pertussis in the presence of a cellulose and/or cellulose derivatives. The present method is useful for obtaining a mixed antigen comprising pertussis toxin and filamentous hemagglutinin in a large amount at low cost. From the antigen, there can be obtained a stable and effective pertussis toxoid to be used for a pertussis vaccine. There is also disclosed a vaccine comprising the pertussis toxoid as an active ingredient and a gelatin and/or gelatin derivatives as a stabilizing agent. The present vaccine is extremely stable and can be stored for a prolonged period of time.
ABSTRACT WORD COUNT: 105

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	EPBBF1	1850
CLAIMS B	(German)	EPBBF1	860
CLAIMS B	(French)	EPBBF1	978
SPEC B	(English)	EPBBF1	9709
Total word count - document A			0
Total word count - document B			13397
Total word count - documents A + B			13397

10/3,AB/39 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0141806 DBR Accession No.: 92-14298
In vitro immunization for the generation of human monoclonal **antibodies** against subcapsular antigens of Neisseria meningitidis B:4P1.15 - **lipopolysaccharide** or outer membrane protein MAb production by in vivo or in vitro immunization of human B-lymphocyte and immortalization by Epstein-Barr virus (conference abstract)
AUTHOR: del Llano M; Fernandez de Cossio M E; Gavilondo J V; del Valle J ; Cruz S; Ohlin M
CORPORATE SOURCE: Division of Immunotechnology and Diagnostics, Center for Genetic Engineering and Biotechnology, P.O. Box 6162, Cubanacan, La Habana-6, Cuba.
JOURNAL: Antibody Eng. (1 pp.) 1991
CODEN: 9999X
LANGUAGE: English
ABSTRACT: The Neisseria meningitidis serogroup B outer membrane proteins (OMPs) and **lipopolysaccharides** (LPSs) are candidates for meningitis therapy. A human monoclonal **antibody** (MAb) was generated against OMP and LIP by Epstein-Barr virus (EBV) immortalization of immunized human B-lymphocytes, followed by fusion with heteromyeloma cells. 2 Human Mabs, IgG1-kappa and IgG3-kappa, recognized the same trypsin-sensitive epitope of class 5 OMP (conserved for serogroups B, Y, A and non-typable, and absent in serogroups Z, X, H, L and K, Haemophilus influenza serotype b, Escherichia coli K1, **Neisseria gonorrhoeae**, and other non-**pathogenic Neisseria** spp.). **LPS** was purified from N. **meningitidis group B**. The in vitro immune response of 14 healthy donors was evaluated using different amounts of antigen. The frequency of positive hetero-hybridoma/number of lymphoblastoid B cells (LCL) increased significantly when positive LCL were selected and

electro-fused 1 wk after EBV infection. Human IgG3-kappa and IgM-kappa MAbs against **LPS** were recognized an epitope on N. meningitidis B:4.P1.15, Vibrio cholera serotype Inaba 569B and Klebsiella pneumoniae. (0 ref)

Set	Items	Description
S11	2	S2 AND LPSS
S12	1	S11 AND ANTIBOD?
S13	0	S12 NOT S9

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14jul04 15:08:06 User219783 Session D2032.3

Search terms

gal(w)E
meningococc? or meningitidis or neisser?
(LPS or ?polysaccharid? or lipopolysaccharid? or LOS or lipo oligosacch?)